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**ADULT IMMUNIZATION**

**A Report By  
The National Vaccine Advisory Committee  
January, 1994**

**National Vaccine Program  
Department of Health and Human Services**

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## EXECUTIVE SUMMARY

Immunization programs in the United States have dramatically reduced the occurrence of many childhood diseases. Several of the classic diseases - diphtheria, pertussis, measles, rubella, and mumps - have been largely controlled. Indigenous poliomyelitis has been eliminated and Hemophilus influenzae type b meningitis is fast disappearing. Nonetheless, the recent resurgence of measles, reports of congenital rubella syndrome, and questions about the safety of pertussis vaccine have been sober reminders of the need for constant vigilance if these diseases are to remain controlled. The nation's response has been an unhesitating commitment to expand our childhood immunization efforts.

The contrast between the occurrence of vaccine-preventable diseases of adults compared with those of children is striking. In the United States fewer than 1000 persons each year die of vaccine-preventable diseases of childhood, whereas 50,000 to 70,000 adults die of influenza, pneumococcal infections, and hepatitis B. The overall costs to society of these and other vaccine-preventable diseases of adults exceed 10 billion dollars each year. Yet adult vaccines are not widely used. Among the reasons given to explain this are (1) limited appreciation of the importance of adult vaccine-preventable diseases; (2) doubts about the safety and efficacy of adult vaccines; (3) the need for selective rather than universal vaccination; (4) different target groups for different vaccines; (5) few organized programs in either the public or private sectors to deliver adult vaccines; and (6) neglect of the reimbursement system for adult immunization. If adult immunization is more complex than childhood vaccination, this does not mean that it has been ignored. Two new vaccines - pneumococcal and hepatitis B - have been introduced in recent years. Many professional organizations have recommended adult vaccines and developed programs for their delivery. And the federal government has taken an active role, most notably in the Medicare Influenza Vaccine Demonstration conducted during the period 1988 to 1992.

Any discussion of adult immunization in the United States must take place within the context of the debate over health care reform. The demonstrated cost-effectiveness of several adult vaccines should add a note of urgency to these discussions. Improving adult immunization will require greater awareness of the importance of vaccine-preventable diseases and the effectiveness and safety of the vaccines. It will require closer working relationships among health care professionals, vaccine manufacturers, and the payers for health care services.

This report of the National Vaccine Advisory Committee describes five major goals for adult immunization in the United States. These goals and 18 recommendations for achieving these goals are set forth in this Executive Summary. The findings that underlie these recommendations and the 72 strategies recommended to achieve the goals are described in the body of this report. None of these goals will be reached without giving attention to all. The task is complex and the effort and resources needed to achieve success will be substantial. In undertaking this work we should remind ourselves that our nation's programs for childhood immunization have reduced the costs of health care and improved the well-being of all our children. We can and should expect no less from our immunization efforts for adults.

**I. GOAL: INCREASE THE DEMAND FOR ADULT VACCINATION BY IMPROVING PROVIDER AND PUBLIC AWARENESS.**

Increasing the demand for adult vaccination must begin with improving the awareness of both health care providers and the general public of the health impact vaccine-preventable diseases and their costs. It will be equally important to improve understanding of the effectiveness and safety of adult vaccines. However, this knowledge must be used in such a way that it leads to changes in behavior -- health care providers to offer vaccines and adults to expect, ask for, and accept recommended vaccines. Programs to increase awareness must not focus simply on increasing content knowledge; i.e., that the diseases are "bad" and the vaccines "good". They must go further and address behaviors that affect vaccine delivery at every level -- the individual, the institution, and society at large.

*I.A. Recommendation: Effective informational programs on adult immunization must be conducted for health care providers on a regular basis to improve their vaccination practices.*

*I.B. Recommendation: Effective information programs must be regularly conducted that educate the public on the importance of vaccine-preventable diseases of adults and the safety and benefits of immunization.*

**II. GOAL: ASSURE THE HEALTH CARE SYSTEM HAS AN ADEQUATE CAPACITY TO DELIVER VACCINES TO ADULTS.**

A highly efficacious vaccine will not be effective in preventing disease unless it is given to those who will benefit. The importance of vaccine delivery has been dramatically demonstrated by the achievements of childhood immunization in the United States. Immunization of almost all children by the time of school entry has been responsible for the elimination of poliomyelitis and the control of other childhood vaccine-preventable diseases. Yet, our nation's inability to adequately vaccinate inner city children was a major factor underlying the recent resurgence of measles.

An adequate capacity to deliver vaccines is as essential for adults as it is for childhood immunization. This requires strong leadership from the Centers for Disease Control and Prevention (CDC), working in collaboration with state and local health authorities. Generalist physicians will remain a major

force in vaccinating adults, but specialist physicians and institutions must recognize their need to become involved in vaccinating special groups of patients. All health care institutions need to adopt and implement guidelines and standards of adult immunization practice. Doing so will reduce the many opportunities that are currently missed to prevent disease through the use of vaccines.

- II.A. Recommendation: The Centers for Disease Control and Prevention and other federal agencies should assume increased responsibility for assuring that adults are immunized. A federal adult immunization grant program separate from childhood immunization programs should be established to assist state and local health departments to improve adult vaccination.
- II.B. Recommendation: All health care providers should be urged to reduce "missed opportunities" for adult immunization.
- II.C. Recommendation: All adults who receive their primary care from general physicians should be appropriately vaccinated.
- II.D. Recommendation: Adults who receive their principal care from specialist physicians, other health care providers or health care institutions should be appropriately vaccinated.
- II.E. Recommendation: Public and private health care systems should develop and implement guidelines and standards for adult immunization practice as part of their quality assurance programs.
- III. **GOAL: ASSURE ADEQUATE FINANCING MECHANISMS TO SUPPORT THE EXPANDED DELIVERY OF VACCINES TO ADULTS.**

Childhood vaccination programs have long received partial financial support from federal, state, and local governments, and the level of support has increased dramatically in recent years. In contrast, the financing of adult immunization has been left largely in the hands of individuals. Coverage for adult immunization services has been largely ignored by health insurance companies. Federal reimbursement for influenza vaccination was specifically prohibited by Medicare regulations until 1993, and inadequately implemented for pneumococcal vaccination since 1981. Although adult immunizations are very inexpensive and remarkably cost-effective compared with most other health care services, they are often ignored by patients and providers alike. Increasing

adult immunization will require adequate public and private financing mechanisms to support vaccine delivery.

*III.A. Recommendation: All publicly funded health insurance programs should adequately reimburse providers for the costs of adult vaccines and their administration.*

*III.B. Recommendation: All private health insurance companies should adequately reimburse providers for the cost of adult vaccines and their administration.*

*III.C. Recommendation: All proposals for national health care reform should include adult immunization services as covered benefits and provide mechanisms to finance their delivery.*

**IV. GOAL: MONITOR AND IMPROVE THE PERFORMANCE OF THE NATION'S VACCINE DELIVERY SYSTEM.**

The nation's ability to control vaccine-preventable diseases requires continuing surveillance of the diseases themselves, an assured manufacturing capacity to provide the vaccines needed, and periodic assessment of whether the vaccines are reaching the persons for whom they are intended. The resurgence of measles during 1989-1991 illustrate the important interplay between these three features of our nation's system for childhood vaccination. The CDC's surveillance system was quick to spot the increase in reported cases of measles, especially in large urban areas. However, the CDC was less effective in monitoring the delivery of measles vaccine to children in the inner-city areas that later became centers of measles outbreaks. It quickly became apparent that minority children, especially Hispanic and black preschoolers, were disproportionately affected by the outbreak. It can be argued that if adequate information on their measles vaccination levels had been available beforehand, vaccination programs could have been organized and the outbreak prevented. Fortunately, the sole U. S. manufacturer was able to provide enough measles vaccine for outbreak control efforts and for the expansion in vaccine use that followed the ACIP's 1989 recommendation that children and certain adults be given a second dose.

*IV.A. Recommendation: Surveillance of vaccine-preventable diseases must be expanded to ensure the effective and efficient use of vaccines in adults.*

IV.B. Recommendation: The capacity of the nation's vaccine manufacturers to meet current and future needs for adult vaccines must be preserved and strengthened.

IV.C. Recommendation: The nation's vaccine delivery system must endeavor to meet the adult immunization goals set forth in Healthy People 2000.

V. GOAL: ASSURE ADEQUATE SUPPORT FOR RESEARCH ON  
(1) VACCINE-PREVENTABLE DISEASES OF ADULTS,  
(2) ADULT VACCINES, (3) ADULT IMMUNIZATION  
PRACTICES, (4) NEW AND IMPROVED VACCINES, (5)  
INTERNATIONAL PROGRAMS FOR ADULT IMMUNIZATION.

Improvements in the control of vaccine-preventable diseases of adults will come from continued research. Understanding the biology of the agents of disease and their interactions with their hosts will suggest new approaches for vaccine development. Research on how vaccines are used in practice will assure that they are given to everyone who will benefit. The complexities of developing new and improved vaccines will require extensive collaboration between individuals and institutions in the public and private sectors. Research on adult vaccines and their use in other countries will expand our understanding of the possibilities for better control of vaccine-preventable diseases of adults throughout the world.

V.A. Recommendation: Research on vaccine-preventable diseases of adults is fundamental to their prevention and must be assured continued support.

V.B. Recommendation: The viability of our nation's adult immunization programs requires evidence of the continued efficacy, safety, clinical effectiveness, cost-benefits and cost-effectiveness of currently available adult vaccines, and research in these areas must be assured adequate support.

V.C. Recommendation: The epidemiology of immunization practices must be better understood if we are to use adult vaccines more effectively and with greater efficiency.

- V.D. Recommendation: The health benefits of adult immunization with several currently available vaccines will be enhanced by improved vaccines and other diseases will become preventable with new vaccines. Research and development of these vaccines must be assured continued and stable support.
- V.E. Recommendation: Research on all aspects of adult immunization must expand to include other developed and developing countries.

## INTRODUCTION

In the United States, the immunization of adults has never received the same attention that has been accorded the immunization of our nation's children. This report seeks to explore some of the reasons for this imbalance. It offers suggestions on how we might extend to greater numbers of adults the protection against vaccine-preventable diseases that we currently provide to our children.

Immunization programs in the United States have dramatically reduced the occurrence of many childhood infectious diseases. Diphtheria and childhood tetanus have practically disappeared, and fatal cases of pertussis, (whooping cough) are rare. No cases of indigenous poliomyelitis have been reported since 1979. The occurrence of measles has also been substantially reduced in spite of the resurgence of disease in 1989-1991. Cases of childhood rubella are rarely observed, and as a result there are few reports of cases of congenital rubella syndrome. Childhood mumps is also a disease rarely encountered by physicians. Finally, within the past few years we have witnessed an extraordinary decline in the occurrence of Hemophilus influenzae type b (Hib) meningitis, an event solely attributable to the introduction and widespread use of Hib vaccines. The results of our childhood immunization programs are summarized in Table 1. These achievements reflect the creativity of our scientists, the enterprise of our vaccine manufacturers, and the commitment of our health care community to guarantee the health and well-being of all our children. Within the past few years, the resurgence of measles, a small but worrisome increase in cases of congenital rubella syndrome, and lingering questions about the safety of pertussis vaccine have been sober reminders that control of vaccine-preventable childhood diseases requires constant vigilance. Our nation's response to these events has been an unhesitating commitment of public and private resources to expand our childhood immunization efforts.

The contrast between the occurrence of adult compared with childhood vaccine-preventable diseases is striking. Each year, fewer than 1000 persons in the United States die of vaccine preventable-diseases of childhood. By comparison, 50,000 to 70,000 adults die of influenza, pneumococcal infections, and hepatitis B (Table 2). In addition, many childhood vaccine-preventable infections are now found among younger adults. Outbreaks of measles, rubella, and mumps have caused major disruptions on college campuses, in the work place, and in institutions such as prisons. These diseases are also important causes of costly hospitalizations. It is estimated

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that 90% or more of all costs of treating pneumococcal infections are the result of hospital care. The overall societal costs of moderately severe influenza outbreaks may be 10 billion dollars or more.

Currently, 98% or more of American children are fully immunized by the time of school entry. Admittedly, the proportion of children fully immunized by the age of two years is much lower, but several initiatives have been established by the federal government and private organizations to address this problem. In contrast, and in spite of the much heavier burden of disease, adult vaccines are not widely used (Table 2). Several reasons have been given to explain these differences. First, there is a limited perception on the part of both health care providers and the general public that adult vaccine-preventable diseases are a significant health problem. Given the much greater incidence of cardiovascular and neoplastic diseases, this perception is not so surprising. Second, there are still doubts in the minds of some health care providers and the public about the efficacy and safety of several adult vaccines. Third, childhood vaccination is universal, whereas adult immunization is selective: different adult vaccines have different target groups. Fourth, the sizes of the target populations for adult immunization vary, and for some vaccines are much larger than the target population for the childhood vaccination (Table 3). Fifth, unlike childhood vaccinations which must be completed if children are to enter school, there are no requirements for adult immunization. Sixth, unlike the child health care practices in most communities throughout the country, there are few widespread and well-organized programs in either the public or private sectors for delivering adult vaccines. Finally, the reimbursement system for adult immunization has been neglected by both government and private insurers, leaving responsibility for paying for vaccination largely in the hands of each individual. Compared with adults there are more opportunities for children to obtain inexpensive or free vaccines from public health clinics. It is the public availability of vaccines, together with responsible parenting and school entry vaccination requirements that has given our nation a high level of childhood immunization. Even in the best of circumstances, it would be difficult to achieve the same immunization levels for adults.

If the circumstances for adult immunization are much more complex than those for childhood vaccination, this does not mean that adult immunization has been ignored. More than ten years ago, two new vaccines for use in adults were licensed: pneumococcal vaccine in 1977 and hepatitis B vaccine in 1983.

The 1980s brought many new initiatives to promote adult immunization. The Advisory Committee on Immunization Practices (ACIP) issued its first recommendations for adult immunization in 1984. The American College of Physicians (ACP) and Infectious Disease Society of America (IDSA) published their first Guide for Adult Immunization in 1985. The U. S. Preventive Services Task Force issued positive evaluations of several adult vaccines and recommended appropriate vaccination of adults of all ages during periodic health examinations. The National Coalition for Adult Immunization (NCAI) successfully worked with Congress to establish National Adult Immunization Awareness Week each October. The American Lung Association and American Thoracic Society launched demonstration projects for influenza vaccination throughout the country. The American College Health Association issued recommendations for vaccines that should be required for college matriculation. The American Hospital Association recommended hepatitis B, rubella, and measles vaccination for health care workers. Finally, in 1988, the Health Care Financing Administration (HCFA) launched its Medicare Influenza Vaccine Demonstration. Over the four-year period from 1988 to 1992, close to \$69 million were spent in a multifaceted program to increase vaccination rates among Medicare enrollees and to evaluate the cost-effectiveness and health benefits of influenza vaccine.

Any discussion of issues related to adult immunization must take place within the context of the debate over health care reform in the United States. There can be no doubt that vaccine-preventable diseases of adults -- chief among them influenza, pneumococcal infections, and hepatitis B -- impose significant health care costs on the nation whenever they are not prevented. The choice our nation faces is not simply one of deciding whether to pay for adult immunization; it is whether to pay more for the costs of treating unprevented illness, or less for preventing it from occurring in the first place. The evidence to date indicates that adult immunization is highly cost-effective. For elderly persons, influenza and pneumococcal vaccines are more cost-effective than all other preventive, screening and treatment interventions that have been studied (Table 4). These considerations should add a note of urgency to any discussion of new initiatives in adult immunization.

Improving adult immunization will require greater awareness of the diseases that can be prevented and of the effectiveness and safety of the vaccines that can be used. It will require closer working relationships among health care professionals, vaccine manufacturers, and payers for health care services. It will require more research at all levels --

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from the laboratory where existing vaccines will be improved and new vaccines created, to the field where innovative programs for vaccine delivery and reimbursement will be evaluated.

This report of the National Vaccine Advisory Committee (NVAC) describes five major goals for adult immunization in the United States. None of the goals will be reached without giving attention to all. The task is complex and the effort and resources needed to achieve success will be substantial. Nevertheless, the effort will be worth the undertaking. Our nation's programs for childhood immunization have reduced the costs of health care and improved the well-being of all our children. We can and should expect no less from our efforts to improve adult immunization.

**OVERVIEW OF THE WORK OF THE  
SUBCOMMITTEE ON ADULT IMMUNIZATION**

This report represents the latest effort of the National Vaccine Advisory Committee to address major issues that affect adult immunization in the United States. It is the outgrowth of work first begun by an earlier NVAC Subcommittee on Adult Immunization. In its February 1990 report, this group set forth eleven recommendations for addressing a series of barriers to adult immunization (Appendix III). These issues were next considered by the NVAC Subcommittee on Access in 1991-1992. During these deliberations it quickly became apparent that access to childhood immunization services would be the Subcommittee's major focus. The many differences between childhood and adult immunization made it difficult to combine the two sets of issues in one report. In December, 1991 it was agreed that a new Subcommittee on Adult Immunization would be formed.

The terms of reference for the Subcommittee on Adult Immunization were prepared in March, 1992 (Appendix IV). The Subcommittee met for the first time on April 22, 1992. The members reviewed an extensive set of background materials prepared by staff of the National Vaccine Program Office and the CDC. The Subcommittee agreed to adopt for its report the structure that was used for the report of the Subcommittee on Access. A set of five goals was proposed and final agreement obtained. At the NVAC's next meeting on November 12-13, 1992 the Subcommittee reviewed a set of proposed recommendations and strategies under each goal, and agreement was obtained shortly thereafter. The final phase of the Subcommittee's work consisted of adding the narrative background for each of the recommendations. The full draft report was reviewed by the Subcommittee at its meeting on September 9-10, 1993. After revision, the final report was presented to the full Committee on January 5-6, 1994.

Throughout its deliberations the Subcommittee has been greatly assisted by staff of the National Vaccine Program Office, (especially Kenneth J. Bart, John Foulds and Daniel A. Lahn) and the CDC's Division of Immunization, now the National Immunization Program (especially Walter W. Williams and Raymond A. Strikas). The Subcommittee has also been helped in its work by the comments of its liaison members: Walter E. Brandt, Elaine C. Esber, William S. Jordan, Walter A. Orenstein, and Regina Rabinovich. The Subcommittee has also benefitted from discussions with a number of outside individuals.

**I. GOAL: INCREASE THE DEMAND FOR ADULT VACCINATION BY  
IMPROVING PROVIDER AND PUBLIC AWARENESS.**

Increasing the demand for adult vaccination must begin with improving the awareness of both health care providers and the general public of the health impact vaccine-preventable diseases and their costs. It will be equally important to improve understanding of the effectiveness and safety of adult vaccines. However, this knowledge must be used in such a way that it leads to changes in behavior -- health care providers to offer vaccines and adults to expect, ask for, and accept recommended vaccines. Programs to increase awareness must not focus simply on increasing content knowledge; i.e., that the diseases are "bad" and the vaccines "good". They must go further and address behaviors that affect vaccine delivery at every level -- the individual, the institution, and society at large.

**I.A. Recommendation:** *Effective informational programs on adult immunization must be conducted for health care providers on a regular basis to improve their vaccination practices.*

**Findings**

In 1980 the Surgeon General's goals for adult immunization for 1990 were published. Among the goals were the following: (1) 60% of all elderly and high-risk persons should be immunized with influenza and pneumococcal vaccines, and (2) 50% of target groups should be vaccinated with new vaccines such as hepatitis B vaccine within five of vaccine licensure. Ten years later these goals had not been reached. They were adopted again as goals for Healthy People 2000.

During the 1980s several sets of recommendations for adult immunization were published, including the ACP/IDSA Guide for Adult Immunization, the ACIP recommendations for adult immunization, and the NCAI Standards for Adult Immunization Practice. Surveys conducted during this period showed that physicians generally had a good understanding of the importance of vaccine-preventable diseases and efficacy and safety of adult vaccines. There was less information on the awareness of other health care professionals such as nurses; but there was good evidence that medical and nursing schools devoted little attention to educating their students about adult immunization. It was also recognized that even if health care providers had a good understanding of the seriousness of the diseases and the

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benefits of vaccination, they often failed to translate their knowledge into clinical practice.

The failure of health care providers to vaccinate patients whom they knew should be vaccinated clearly showed that knowledge about vaccination practices and how to improve them was every bit as important as knowledge about the diseases and their vaccines. In the 1980s many studies demonstrated that the administrative and organizational features of vaccination programs were the keys to their success. For example, modifying a computer program used for discharging patients from the hospital increased pneumococcal vaccination rates from < 5% to approximately 50%. Developing an institution-wide program for influenza vaccination in a Veterans Affairs hospital increased vaccination rates among outpatients to 60% (the Surgeon General's goal) and among inpatients to almost 80%. Nursing homes that considered influenza vaccination to be part of routine medical care and did not require specific written consent by or on behalf of individual residents had much better vaccination rates than institutions which did require consent. Target-based programs for influenza vaccination in physicians' offices reliably resulted in higher vaccination rates. For each of these approaches to vaccination the specific features varied greatly. What was common to each was a decision that was made, often by one or two individuals, to develop an organized approach for offering vaccines on a regular basis. In some of these programs increased numbers of physicians, nurses, and other health care providers themselves were also vaccinated.

### Strategies

- o Promote widespread distribution of the adult immunization goals set for them in Healthy People 2000; recommendations for specific vaccines issued by the Advisory Committee on Immunization Practices (ACIP), the "Standards for Adult Immunization Practice" developed by the National Coalition for Adult Immunization; and the vaccination recommendations of other professional groups.
- o Periodically assess the knowledge and attitudes of physicians, nurses, and other health care providers and students regarding vaccine-preventable diseases of adults, the efficacy and safety of adult vaccines, and provider behavior in offering vaccines to adults.

- Encourage greater emphasis on adult immunization in the professional education of health care providers and in their licensure and certifying examinations.
- Determine which administrative innovations, organizational changes, and motivational factors are effective in ensuring the delivery of adult vaccines.
- Emphasize practical approaches to vaccine delivery in training programs for health care providers that build a foundation for effective immunization practices throughout their professional careers.
- Urge all health care providers to be appropriately immunized as students and trainees and to keep their immunizations appropriately updated in order to protect both themselves and their patients.

I.B. Recommendation: *Effective information programs must be regularly conducted that educate the public on the importance of vaccine-preventable diseases of adults and the safety and benefits of immunization.*

### Findings

Better public understanding of the seriousness and vaccine-preventable diseases and the benefits of vaccination will be essential if there are to be improvements in adult immunization. Lack of knowledge about the diseases themselves is perhaps the greatest barrier. Many elderly patients fail to appreciate that influenza presents a very real risk of severe illness that may lead to hospital admission or death. Even more have no knowledge of the frequency or severity of pneumococcal infections. Most younger adults who have had several sexual partners have no understanding of their risk for acquiring hepatitis B.

Many adults also fail to appreciate the high degree of clinical effectiveness and safety of adult vaccines. This is particularly true for influenza vaccine. For many older adults opinions about adverse reactions formed more than 20 years ago have not changed, although newer vaccines have been developed that are virtually free of major side effects.

Educational programs can help increase public understanding of the need for and benefits of adult immunization. The efforts of physicians, nurses, and other health care workers to educate individual patients cannot be

forgotten, but larger efforts that target groups of patients or even large populations must also be considered. The importance of these larger efforts was illustrated recently during the HCFA Medicare Influenza Vaccine Demonstration; a letter sent to each Medicare enrollee in the study from the HCFA Administrator was regarded as one of the most effective interventions in helping to persuade older persons to get vaccinated. In other developed countries in Europe and North America, media campaigns conducted by professional organizations working with vaccine manufacturers have been successful in increasing rates of influenza vaccination. In France, where the rate of influenza vaccine use is higher than it is in the United States, the social security checks sent to elderly retirees each October include a voucher for a free dose of influenza vaccine.

#### Strategies

- o Periodically assess the knowledge and attitudes of adults in target populations regarding vaccine-preventable diseases and the benefits and risks of vaccination.
- o Determine which factors constitute barriers or promote easy access to adult immunization and develop strategies to overcome these barriers and improve access.
- o Implement effective and efficient media campaigns and educational programs to motivate adults in target populations to be vaccinated.
- o Link educational and promotional programs for adult immunization with other announcements routinely directed to target populations by community organizations and government agencies.

#### **II. GOAL: ASSURE THE HEALTH CARE SYSTEM HAS AN ADEQUATE CAPACITY TO DELIVER VACCINES TO ADULTS.**

A highly efficacious vaccine will not be effective in preventing disease unless it is given to those who will benefit. The importance of vaccine delivery has been dramatically demonstrated by the achievements of childhood immunization in the United States. Immunization of almost all children by the time of school entry has been responsible for the elimination of poliomyelitis and the control of other

childhood vaccine-preventable diseases. Yet, our nation's inability to adequately vaccinate inner city children was a major factor underlying the recent resurgence of measles.

An adequate capacity to deliver vaccines is as essential for adults as it is for childhood immunization. This requires strong leadership from the Centers for Disease Control and Prevention (CDC), working in collaboration with state and local health authorities. Generalist physicians will remain a major force in vaccinating adults, but specialist physicians and institutions must recognize their need to become involved in vaccinating special groups of patients. All health care institutions need to adopt and implement guidelines and standards of adult immunization practice. Doing so will reduce the many opportunities that are currently missed to prevent disease through the use of vaccines.

*II.A. Recommendation: The Centers for Disease Control and Prevention and other federal agencies should assume increased responsibility for assuring that adults are immunized. A federal adult immunization grant program separate from childhood immunization programs should be established to assist state and local health departments to improve adult vaccination.*

### Findings

The history of childhood vaccination in the United States over the past two decades has provided overwhelming evidence of the leading role played by the CDC in improving vaccination rates among our nation's children. Today, approximately half of all children receive their basic childhood immunizations through state and local public health programs. These programs use vaccines purchased under federal contracts negotiated by the CDC. Investigators at the CDC conduct epidemiologic studies of the occurrence of vaccine-preventable diseases and the susceptibility of children to infection. The CDC played a leading role in persuading states to establish vaccination requirements for children prior to school entry. As much as anything else, these requirements have been our best guarantee that children are fully vaccinated against childhood diseases.

For many years CDC staff have been responsible for evaluating our nation's vaccination programs. The recent experience with the resurgence of measles demonstrated shortcomings in our childhood vaccination efforts: many children, especially those who were poor and lived in inner

city areas, had not completed their primary immunizations on schedule and as a result became infected. Research by CDC investigators uncovered many barriers to effective delivery of childhood vaccines: inadequate staffing of public clinics, limited hours of operation, unnecessary requirements for scheduled appointments or for complete physical examinations. In response to the CDC's evaluation, an Infant Immunization Initiative has been established. This initiative will provide additional staff and other resources for childhood vaccination at the state and local level as well as at the CDC. Efforts will be undertaken to coordinate the activities of several governmental agencies involved in health-related activities (e.g., WIC programs) to ensure timely vaccination. The federal contract mechanism for the purchase and distribution of childhood vaccines will be greatly expanded.

The recently concluded Medicare Influenza Vaccine Demonstration represents another vaccine delivery program that has been successfully coordinated by the CDC. Working in collaboration with HCFA, CDC staff helped implement a multifaceted project that included (1) federal contract purchase of influenza vaccine, (2) distribution of vaccine free-of-charge to physicians, nursing homes, public clinics, hospitals, and HMOs, (3) public and provider education, and (4) reimbursement of providers for vaccine administration.

The CDC staff have developed a wide range of skills and experience in coordinating public sector vaccine delivery programs for children throughout the nation. Given additional resources the CDC is capable of providing similar leadership for coordinating a broad range of public programs for adult immunization.

### Strategies

- o Provide increased staff and support to the Centers for Disease Control and Prevention to expand its adult immunization activities and its assistance to state and local adult immunization programs.
- o Ensure that public health clinics and state and local health agencies can provide adult immunization services that are inexpensive or cost-free to patients and that are offered at convenient times and in easily accessible locations.
- o Provide federal grants to support vaccine purchase and program administration at the state and local level.

- o Provide adequate support for the adult immunization programs of the Department of Veterans Affairs, Department of Defense, and other federal agencies.

II.B. Recommendation: All health care providers should be urged to reduce "missed opportunities" for adult immunization.

### Findings

One of the important findings to come out of research on vaccination practices over the past decade has been the observation that the great majority of children and adults who develop vaccine-preventable illnesses have been seen previously by health care providers, could have been vaccinated at the time, but were not. Such "missed opportunities" for vaccination have several causes. Physicians who are asked by patients to deal with complaints seldom hear their patients complain that they have not been vaccinated. Vaccinating many patients when only one or two obtain real benefits may not seem to be a sensible investment of a physician's time or energies compared with taking care of the real problems each patient brings to the encounter. The past history of vaccination may be unknown to both the patient and the physician, and obtaining accurate documentation may be too troublesome. Misconceptions regarding what are and are not valid contraindications to vaccination are especially common. Finally, even when knowledge and motivation are high, there may be no organized approach to make sure that every person who needs a vaccine actually has it offered.

It has been said repeatedly that the failure to prevent vaccine-preventable diseases is far more often due to the failure to vaccinate and not to the failure of the vaccines themselves. The price for these errors of omission can be very high.

### Strategies

- o Educate all health care providers to recognize that any contact with a provider should be considered an opportunity to provide needed vaccines.
- o Include information on misconceptions regarding contraindications to vaccination in educational programs on adult immunization.

II.C. Recommendation: All adults who receive their primary care from general physicians should be appropriately vaccinated.

#### Findings

Most vaccines given to adults are administered by primary care physicians. For example, according to the results of the United States Immunization Survey, in the early 1980s up to 80% of influenza vaccinations were given by generalist physicians. Yet wide variations have been demonstrated when the immunization practices of individual physicians have been compared. Organized interventions such as "target-based" influenza vaccination of elderly persons can be very effective in increasing vaccine delivery by all physicians. However, improving vaccination practices for influenza may be relatively easy because the vaccine must be given every year. For other vaccines that are given much less frequently, selecting patients can be more difficult; e.g., persons with multiple sexual partners or intravenous drug users who need hepatitis B vaccine. No matter how knowledgeable physicians and other health care providers may be about whom to vaccinate, vaccines are regularly offered to patients only when programs have been established for doing so.

#### Strategies

- o Ensure that the primary health care of adults includes periodic assessment of their needs for vaccines based on age, occupation, situation and life style.
- o Encourage providers to have accurate and accessible medical records, periodic reminder systems, and other administrative and organizational arrangements to guarantee the regular offering of vaccines to adult patients.

II.D. Recommendation: Adults who receive their principal care from specialist physicians, other health care providers or health care institutions should be appropriately vaccinated.

#### Findings

Many adults who are in greatest need of vaccination receive their principal care from specialist rather than generalist physicians. Often their care is provided by highly

specialized teams of health care professionals (e.g., the staff of a hemodialysis unit). Sometimes care is provided more by an administrative unit such as clinic or even by an entire institution such as a hospital. In such settings a single focus of responsibility for acute care is often difficult to identify. Thus, it should not be surprising to find the same thing to be true for preventive care such as vaccination.

It has been shown recently that for several vaccine-preventable diseases, persons at greater risk of becoming seriously ill are less likely to be vaccinated. For example, patients discharged from hospitals are at greatly increased risk of being readmitted with influenza or pneumococcal infections compared with nonhospitalized persons, but are less likely to be vaccinated. In contrast, health care workers account for < 5% of new cases of hepatitis B infection, yet they have received more than 80% of the hepatitis B vaccine that has been given.

The concept of primary care is central to all discussions of health care reform. Yet it would be a mistake to assume that adult immunization should be the exclusive responsibility of primary care physicians. More often than not, persons in greatest need of vaccination have a specialist physician who provides their principal care. Sometimes these patients have no physician at all. Thus, efforts to improve the delivery of adult vaccines must focus on developing workable systems for regularly offering vaccines to patients at risk who are cared for in specialist settings or institutions, whether it be in a hospital, a nursing home, a clinic for sexually-transmitted diseases, or an emergency room.

### Strategies

- o Urge specialist physicians (e.g., cardiologists, pulmonologists, hematologists, oncologists, endocrinologists, and nephrologists in dialysis centers) who are the principal providers of health care to certain adults to offer their patients vaccines when indicated.
- o Urge hospitals that care for adults to provide adult immunization services on inpatient units and in emergency rooms and clinics.
- o Assure that nursing homes provide recommended vaccines to all their residents.

- o Encourage visiting nurses and other community and home health care providers to offer vaccines to home-bound adults and adults in other settings (e.g., retirement homes).
- o Develop specific programs for vaccinating hard-to-reach adults at increased risk of vaccine-preventable diseases (e.g., homeless persons, IV drug users, persons attending STD clinics).

II.E. Recommendation: *Public and private health care systems should develop and implement guidelines and standards for adult immunization practice as part of their quality assurance programs.*

### Findings

One of the most noteworthy new features in health care delivery has been the development of guidelines for clinical practice. Often criticized as "cookbook medicine", practice guidelines attempt to make explicit the very best in clinical reasoning and to do so in ways that can be applied to all patients, regardless of who the health care provider may be. Practice guidelines are becoming an increasingly common feature of quality assurance programs in hospitals and in managed care settings. Often these programs have been mandated by health insurers as part of their cost containment efforts.

The first "Standards for Adult Immunization Practice" were developed voluntarily by the National Coalition for Adult Immunization and published in 1990 (Appendix II). Several state legislatures have gone one step further and established regulations that require nursing homes to offer influenza vaccine to all of their residents. In the next few years it is likely that organizations responsible for the accreditation of health care institutions will require them to develop and monitor programs for offering vaccines to their adult patients.

### Strategies

- o Require federal, state and local health care institutions to develop and monitor systems for assuring that eligible adults are offered the vaccines they need.
- o Support administrative and legislative policies that require health care institutions to offer vaccines to adults.

- o Encourage the Joint Commission on the Accreditation of Health Care Organizations and other accrediting organizations to require hospitals, nursing homes, managed care organizations, clinics and physicians' offices to develop and monitor systems for assuring adult immunization.

**III. GOAL: ASSURE ADEQUATE FINANCING MECHANISMS TO SUPPORT THE EXPANDED DELIVERY OF VACCINES TO ADULTS.**

Childhood vaccination programs have long received partial financial support from federal, state, and local governments, and the level of support has increased dramatically in recent years. In contrast, the financing of adult immunization has been left largely in the hands of individuals. Coverage for adult immunization services has been largely ignored by health insurance companies. Federal reimbursement for influenza vaccination was specifically prohibited by Medicare regulations until 1993, and inadequately implemented for pneumococcal vaccination since 1981. Although adult immunizations are very inexpensive and remarkably cost-effective compared with most other health care services, they are often ignored by patients and providers alike. Increasing adult immunization will require adequate public and private financing mechanisms to support vaccine delivery.

*III.A. Recommendation: All publicly funded health insurance programs should adequately reimburse providers for the costs of adult vaccines and their administration.*

**Findings**

More than two decades of experience with publicly funded vaccination programs for children have demonstrated the strengths and weaknesses of the relationships between federal agencies and state and local health departments. For many years the CDC has administered a system for purchasing childhood vaccines under a federal contract. Vaccines purchased under this system have been distributed to state and local health departments. Children are vaccinated either free of charge or for only a small fee to cover the costs of vaccine administration. Successful as this program has been, it has not reached all of the children who depend on it. In 1994, the federal government will expand this program so childhood vaccines purchased with federal funds will be made available to virtually all children in the United States for

whom private payment or insurance coverage for vaccination are unavailable.

Compared with childhood vaccination, public agencies at the federal, state, and local level have been much less involved with adult immunization. Although many state and local health departments have purchased modest amounts of influenza vaccine or, less commonly, pneumococcal vaccine for use in public clinics, there has been no federal contract to purchase adult vaccines in bulk for these programs. As a result, in 1991 less than 10% of all doses of influenza and pneumococcal vaccines distributed in the United States were distributed through state and local health departments. In 1981 Congress instructed the Health Care Financing Administration to pay physicians for pneumococcal vaccination of elderly patients under Part B of the Medicare program. In 1984 this program was expanded to include hepatitis B vaccination for Medicare patients with end-stage renal disease. At the conclusion of the Medicare Influenza Vaccine Demonstration in 1993, Medicare was authorized to pay for influenza vaccine and its administration.

The implementation of these Medicare reimbursement programs for vaccination has not measured up to their promise. Pneumococcal vaccination illustrates some of the problems encountered. During each of the ten years following the introduction of Medicare reimbursement in 1981, fewer doses of pneumococcal vaccine were distributed nationwide than during each of the years that preceded it. The program's shortcomings were probably caused by several factors. Medicare fiscal intermediaries may not have been fully informed about it. There was a Medicare billing code to cover the cost of the vaccine itself, but no billing code to cover the cost of its administration. The reimbursement level for the vaccine was so close to what physicians had to pay for it that many physicians actually lost money billing Medicare for pneumococcal vaccination. Not surprisingly, only 300,000 to 400,000 doses of vaccine -- 25% of all doses distributed nationwide each year -- could be accounted for by the Medicare reimbursement program.

The recent extension of Medicare reimbursement to cover influenza vaccination is expected to generate 10 to 15 million vaccination claims each year. HCFA has recently developed billing codes for physicians and other health care providers so they can bill both for influenza vaccine and for its administration. The size of this new program dwarfs the Medicare reimbursement programs for pneumococcal and hepatitis B vaccines. Failure on the part of providers and/or third

party fiscal intermediaries to understand and implement this new program will be highly visible. It will be important that it be monitored closely to ensure that reimbursement levels are adequate and that billing procedures are understood by payers and providers alike. Monitoring should also include reimbursement for pneumococcal and hepatitis B vaccination of Medicare enrollees.

### Strategies

- o Periodically assess Medicare and Medicaid reimbursement rates to assure that they adequately compensate providers for adult immunization services.
- o Determine whether federal reimbursement policies for adult immunization are understood and properly implemented by third party fiscal intermediaries and providers.
- o Provide technical assistance where necessary to third party fiscal intermediaries and provider representatives to ensure full implementation of federal reimbursement policies for adult immunization.
- o Assure that all adult beneficiaries of federally financed health care services are not denied coverage for immunizations recommended by the ACIP.
- o Determine whether financial or other incentives to public providers can ensure high rates of vaccine delivery to adults.

*III.B. Recommendation: All private health insurance companies should adequately reimburse providers for the cost of adult vaccines and their administration.*

### Findings

There is little reliable information on the extent to which private health insurance companies include adult immunization among their covered benefits. Even less is known about levels of reimbursement and requirements for cost-sharing by patients. Health maintenance organizations may include adult immunization services among their covered benefits, but in many HMOs immunization rates are generally no better than they are among patients covered by traditional health insurance. Some businesses offer immunizations, especially

influenza vaccination, to their employees. It is uncertain whether these programs improve productivity or are cost-effective, although the health benefits may be substantial. Whether state regulators of health insurance companies have actively sought to have insurers cover adult vaccination services is also unknown. The increasing tendency for businesses to self-insure, and thus not be subject to regulation by state governments, suggests that reliance on regulatory approaches to improve coverage of adult immunization may not be sufficient.

### Strategies

- o Encourage the health care insurance industry to develop, offer, and promote benefit packages that provide full reimbursement for adult immunization without requiring copayments or deductibles.
- o Encourage business and labor leaders to include adult immunization services as essential features of the health care benefits provided to employees.
- o Encourage state health insurance regulatory agencies to require that private health insurers include adult immunization as a covered benefit.
- o Encourage companies that self-insure their employees to provide adult immunization as a covered benefit.
- o Determine whether financial or other incentives to private providers can assure high rates of vaccine delivery to adults.

*III.C. Recommendation: All proposals for national health care reform should include adult immunization services as covered benefits and provide mechanisms to finance their delivery.*

### Findings

General discussions of health care reform emphasize the importance of preventive services. Specific proposals usually include broadened coverage for immunization, especially for children. As the national debate on health care reform begins to focus on a few alternatives, it will be important to examine the provisions for adult immunization in each proposal. At a minimum, Medicare reimbursement for influenza, pneumococcal and hepatitis B vaccination of Medicare enrollees must be

preserved. Individual proposals that expand immunization coverage to other groups of adults must be compared. Proposals that include cost sharing by patients must be analyzed to determine what effects this might have on vaccination rates for individual vaccines and on their cost effectiveness.

#### Strategies

- o Undertake studies that examine the economic implications of insuring adult immunization services in competing proposals for reform of health care financing.
- o Explore the potential impact of competing proposals for health insurance reform on vaccination rates for adults.

#### **IV. GOAL: MONITOR AND IMPROVE THE PERFORMANCE OF THE NATION'S VACCINE DELIVERY SYSTEM.**

The nation's ability to control vaccine-preventable diseases requires continuing surveillance of the diseases themselves, an assured manufacturing capacity to provide the vaccines needed, and periodic assessment of whether the vaccines are reaching the persons for whom they are intended. The resurgence of measles during 1989-1991 illustrate the important interplay between these three features of our nation's system for childhood vaccination. The CDC's surveillance system was quick to spot the increase in reported cases of measles, especially in large urban areas. However, the CDC was less effective in monitoring the delivery of measles vaccine to children in the inner-city areas that later became centers of measles outbreaks. It quickly became apparent that minority children, especially Hispanic and black preschoolers, were disproportionately affected by the outbreak. It can be argued that if adequate information on their measles vaccination levels had been available beforehand, vaccination programs could have been organized and the outbreak prevented. Fortunately, the sole U. S. manufacturer was able to provide enough measles vaccine for outbreak control efforts and for the expansion in vaccine use that followed the ACIP's 1989 recommendation that children and certain adults be given a second dose.

*IV.A. Recommendation: Surveillance of vaccine-preventable diseases must be expanded to ensure the effective and efficient use of vaccines in adults.*

#### Findings

The effective and efficient use of vaccines in adults depends on a clear understanding of which vaccine-preventable diseases are epidemiologically important and which groups of people are at risk of becoming infected. For many years the CDC has worked closely with state and local health agencies to monitor the occurrence of influenza and identify the viruses responsible for community outbreaks. By analyzing information gathered from throughout the nation, the CDC has provided timely advice on the identity of the virus strain causing disease, offered reassurance on whether the current year's influenza vaccine can be expected to confer protection, and made recommendations on whether antiviral chemoprophylaxis and chemotherapy are likely to be of benefit. The CDC's epidemiologic assessment of influenza in the United States is shared with health officials at the World Health Organization and contributes to an understanding of the global occurrence of influenza.

For the other vaccine-preventable diseases of adults, the surveillance efforts of the CDC and state and local health departments are less extensive. Detailed surveillance in a few cities and counties has provided some understanding of the epidemiology of pneumococcal infections and hepatitis B, but these efforts have been limited and may have failed to identify important population groups at increased risk of infection.

Surveillance programs could be enhanced if inexpensive methods were developed that permit rapid diagnosis of disease. Better tests could allow these programs to be more population-based than they currently are. Surveillance programs also need to include studies of the economic impact of vaccine-preventable diseases. Understanding the opportunity costs of unprevented disease can provide the basis for planning more efficient use of adult vaccines.

#### Strategies

- o Maintain and strengthen the Centers for Disease Control and Prevention's national and international surveillance programs for vaccine-preventable diseases.

- o Assist state and local efforts to conduct surveillance programs for vaccine-preventable diseases.
- o Support research and development of rapid, inexpensive methods to improve the diagnosis and surveillance of vaccine-preventable diseases.

IV.B. Recommendation: *The capacity of the nation's vaccine manufacturers to meet current and future needs for adult vaccines must be preserved and strengthened.*

### Findings

The success of our nation's immunization programs for children and adults depends on the capacity of our vaccine manufacturers to produce and distribute a constant supply of vaccine products. However, as was shown in 1976, the limits of our system for vaccine supply can be severely tested. The swine influenza vaccine program required that vaccine manufacturers produce within a matter of months approximately 150 million doses of swine influenza vaccine -- an amount six to seven times greater than the number of doses usually supplied. Several decisions helped to make this goal achievable. Most of the vaccine was supplied as a monovalent preparation (i.e., it did not contain an influenza B virus component). Also, the antigenic content per dose was approximately half the content of previous years' vaccines. However, these technical matters were overshadowed by the much larger issue of liability. Given the uncertainties of this enormous program, the vaccine manufacturers were reluctant to assume sole responsibility for claims from vaccine recipients for vaccine-associated adverse reactions. The swine influenza vaccine program did not go forward until it was agreed that the federal government would underwrite the costs of settling claims for vaccine-associated injury. The importance of this decision became evident when the program was later suspended following reports of a few cases of Guillain-Barré syndrome in persons who had been vaccinated. Over the next several years, vaccine injury claims amounting to several billion dollars were filed. It is difficult to imagine how the vaccine manufacturers could have handled these claims on their own.

In the 1980s, liability issues related to pertussis vaccination were the driving force behind the rapid rise in the costs of childhood vaccines. This cost increase was an important contributor to the decline in the numbers of children who received their vaccines according to the recommended time schedule and to the increase in those who were forced to seek

vaccination in public clinics. Liability issues also posed a serious threat to the economic viability of the vaccine manufacturers. There was serious discussion that some of them might be forced to cease vaccine production. The creation of the National Vaccine Injury Compensation Program in 1986 provided a new mechanism by which claims for vaccine-associated injury could be settled. Although implementation of this program has been costly and not without problems, it has succeeded in stabilizing the market for the vaccine manufacturers.

This past year new proposals that have called for the federal government to play a much larger role in the purchase and distribution of childhood vaccines have been met by serious objections from vaccine manufacturers. The debate on the merits of these proposals has been sharp and widely reported. Recent legislation will provide funds for an expanded program of federal purchase of childhood vaccines for children on Medicaid and those who lack health insurance. This program reflects an uneasy compromise between the manufacturers who argue that a market-based approach for the purchase of vaccines is the best guarantee of their future supply and advocates of public purchase who argue that lower vaccine costs are necessary to ensure higher vaccination rates for children.

The experiences with the swine influenza vaccine program in the 1970s and with vaccine liability in the 1980s demonstrate some of the shortcomings of the way we address important issues affecting our capacity to meet current and future needs for vaccines. We have often reacted to crises instead of anticipating problems in advance. Given the technical, regulatory, legal and political complexity of these problems, this may be understandable but it is not a satisfactory approach to their solution. Problems of vaccine supply are certain to arise in the future. Several can already be anticipated: the threat of a new influenza pandemic, the need for less expensive hepatitis B vaccines to ensure universal childhood immunization, the possibility that more widespread or even universal immunization with pneumococcal vaccine may become necessary as antimicrobial-resistance of pneumococcal organisms becomes widespread, and the need for vaccines against newly emergent pathogens. To successfully meet these challenges will require more thoughtful planning than we have had in the past.

### Strategies

- o Periodically assess the ability of the nation's vaccine manufacturers to supply vaccines in quantities sufficient to meet the needs of adults, identifying potential technical, regulatory, financial, legal or political problems that might compromise their ability to do so.
- o Assess the capacity of the nation's vaccine manufacturers to respond to urgent demands for increased supplies of an existing vaccine or a new vaccine.
- o Establish mechanisms for public health officials and the nation's vaccine manufacturers to assess and resolve short- and long-term vaccine supply issues.
- o Explore the technical, regulatory, legal and political problems that might be encountered if it becomes necessary to obtain one or more adult vaccines from a foreign supplier.
- o Determine the advantages and disadvantages of federally financed bulk purchase, federal contracting of production, or federal production of one or more vaccines and their distribution to public and private health care providers.
- o Explore the advantages and disadvantages of incorporating accepted vaccine-related adverse events which follow adult immunization into the National Vaccine Injury Compensation Program.

IV.C. Recommendation: *The nation's vaccine delivery system must endeavor to meet the adult immunization goals set forth in Healthy People 2000.*

### Findings

The adult immunization goals set forth in Healthy People 2000 are the same as the goals that were established for 1990. One reason we failed to achieve these goals by 1990 is that in order to improve our performance in vaccine delivery we first have to monitor what we have been doing. We have not monitored our adult immunization practices very well.

Beginning in the late 1960s, the United States Immunization Survey provided useful information on influenza vaccination levels on an annual basis. For several reasons the survey was discontinued in 1985. During the next three years, occasional surveys provided limited information on influenza and, to a lesser extent, pneumococcal vaccination rates for elderly persons. However, starting in 1989, the National Center for Health Statistics began to gather information on vaccination rates against influenza, pneumococcal disease, tetanus and diphtheria. This information is now obtained on a biennial basis through questions that have been added to the National Health Interview Survey. Earlier serologic studies of antibody levels to tetanus, diphtheria, measles, and rubella, however, provided sobering reminders of the vulnerability of millions of adult Americans to vaccine-preventable diseases. In spite of recent progress, we still know very little about our efforts to ensure protection against these diseases by vaccinating susceptible adults.

The little information we have on the epidemiology of adult immunization usually provides figures for the population as a whole rather than for particular high-risk groups. For example, we have learned from surveys that only 20 percent of the elderly have ever received pneumococcal vaccine, but we know nothing about geographic variations in the use of the vaccine, nor about vaccination rates in certain groups of elderly persons that may be at greatly increased risk of disease. This is an important issue: a recent study has shown that persons at greater risk of influenza-associated hospitalization and death are actually less likely to be given influenza vaccine than persons at lower risk. For other vaccines such as hepatitis B vaccine, we have a great deal of information about the vaccination status of health care workers, but almost no information on the vaccination status of the other groups of high-risk individuals that account for more than 95% of the disease. We know more about measles antibody levels and measles vaccination programs among younger adults who attend colleges than among those who do not. We have little information on the variations in vaccination rates among different minority or socioeconomic groups, although a recent study has shown that persons who are poor and black have both higher rates of pneumococcal disease and lower rates of pneumococcal vaccination. Other studies have shown that identifying high-risk patients on the basis of the presence or absence of underlying medical conditions may be less useful than defining them according to the kinds of medical care they have received for these conditions; i.e., patients with previous hospital care for heart disease are at greater risk

for influenza-associated hospital admission than are heart disease patients who have not required hospitalization.

Recent experience suggests that administrative databases can be used to monitor immunization activities in large populations. In Canada, the use of databases that are linked to other data sets (e.g., population registries, hospital discharge abstracts) has provided useful information on the epidemiology of immunization practices. Such systems provide the means not only to monitor vaccination practices in populations, but also to target vaccination reminders to persons who have not been vaccinated but should be. In the United States, HCFA data files have similar potential for monitoring the delivery of influenza and pneumococcal vaccines, analyzing variations in vaccination practices, and targeting special interventions for groups of Medicare patients at increased risk. For other groups that are poor and lack health insurance, Medicaid data files have similar potential for monitoring and improving vaccine delivery to high-risk adults.

#### Strategies

- o Regularly assess adult immunization levels through the National Health Interview Survey (NHIS).
- o Periodically assess vaccination rates in target populations for individual adult vaccines, including persons with specific high-risk conditions (e.g., cardiopulmonary disease) and special groups at risk (e.g., pregnant women, HIV-infected individuals).
- o Use administrative systems for billing for immunization services to monitor vaccination rates of adults enrolled in federal and nonfederal health care programs.
- o Increase surveillance of adult immunization in areas or in population groups where vaccination rates are unsatisfactory and determine why this has occurred.
- o Establish federally funded demonstration projects to increase the delivery of adult vaccines in areas or among population groups where vaccination rates have been determined to be unsatisfactory.

- V.       **GOAL:**     **ASSURE ADEQUATE SUPPORT FOR RESEARCH ON**  
                  **(1) VACCINE-PREVENTABLE DISEASES OF ADULTS,**  
                  **(2) ADULT VACCINES, (3) ADULT IMMUNIZATION**  
                  **PRACTICES, (4) NEW AND IMPROVED VACCINES, (5)**  
                  **INTERNATIONAL PROGRAMS FOR ADULT IMMUNIZATION.**

Improvements in the control of vaccine-preventable diseases of adults will come from continued research. Understanding the biology of the agents of disease and their interactions with their hosts will suggest new approaches for vaccine development. Research on how vaccines are used in practice will assure that they are given to everyone who will benefit. The complexities of developing new and improved vaccines will require extensive collaboration between individuals and institutions in the public and private sectors. Research on adult vaccines and their use in other countries will expand our understanding of the possibilities for better control of vaccine-preventable diseases of adults throughout the world.

- V.A.    Recommendation:   *Research on vaccine-preventable diseases of adults is fundamental to their prevention and must be assured continued support.*

### Findings

Basic research on the viruses and bacteria that cause disease is essential if we are to develop new and improved vaccines for adults. Several diseases may eventually become preventable once the biology of their causative agents is understood. For example, Mycoplasma pneumoniae is a common cause of pneumonia in adults. Little is known about the pathogenesis of disease and the biological basis for the microorganism's ability to alter its properties and evade host defenses. A mycoplasma vaccine would be of enormous benefit. For hepatitis C, there is little understanding of how infection is acquired in almost half of cases, why 70% of patients who are infected fail to recover completely and become chronic carriers, and why primary infection fails to protect against repeat hepatitis C infection. There can be little hope of developing a hepatitis C vaccine until these fundamental questions are answered. For tuberculosis, the need to return to basic research on the agent of disease has become urgent. The decades-long decline in the occurrence of disease came to a halt in 1985, and by 1992 the number of reported cases of active disease in the United States had increased by 20%. Many of these infections have been caused by multidrug-resistant strains of M. tuberculosis. New studies are needed to develop improved laboratory model systems to support basic and applied research, to determine basic mechanisms of drug resistance, and to identify factors that determine the organism's infectivity

and virulence. Success will have direct bearing on the development of a better vaccine against tuberculosis.

Basic research on the host response to infection and to vaccination is as important as research on the agents of disease. This is particularly important for elderly adults whose immune systems become less responsive with advancing age. Studies exploring mechanisms to overcome this immune senescence such as the use of adjuvants and hormones are in their infancy. Better understanding of host defenses at the mucosal surfaces of the respiratory, gastrointestinal and genitourinary tracts is of particular importance. The problems facing the development of vaccines for sexually transmitted diseases illustrate these difficulties. The biology of the multifaceted variability of Neisseria gonorrhoea is only slowly being unraveled. Recently it has been discovered that the immune response to chlamydial infections can be both deleterious and protective. The complex relationship between chronic Herpes simplex virus type 2 and human papilloma virus infections and the host cell presents a formidable challenge to investigators. Whether an effective immune response against any one of these agents can be generated at the mucosal surface of the genitourinary tract through vaccination, and if so by what route is still unknown. However, the need for effective vaccines against sexually transmitted diseases has already become urgent with the recognition of their important role in facilitating the transmission of human immunodeficiency virus (HIV) infection.

Along with basic research on the microbiology and immunology of current and future vaccine-preventable diseases, much more needs to be learned about their impact on adult populations. More information is needed on the health and economic consequences of influenza and pertussis on working adults and their families. Sensible use of new vaccines such as the Ty21a and Vi antigen typhoid vaccines among international travellers will require a clear understanding of whether their potential health benefits will be worth their costs. Whether the higher incidence of disease and lower rate of immunization that has been shown for pneumococcal disease and pneumococcal vaccination among minority groups applies to other adult vaccine-preventable disease requires careful examination. The health and economic impact of Lyme disease must be understood before a vaccine is licensed if we are to know how best to use it.

### Strategies

- o Support research on microbiologic agents that cause vaccine-preventable diseases in adults.

- o Support research on the host response to vaccine-preventable diseases of adults, including immunocompromised and aging individuals.
- o Expand studies that seek to enhance the immune response to vaccination, including the response of immunocompromised and elderly patients.
- o Develop better measures of the direct and indirect costs of vaccine-preventable diseases of adults, including their impact among working adults, special populations at risk (e.g., health care workers, international travelers), and different socioeconomic groups.
- o Conduct research on the health and economic impact of adult diseases that may become preventable by vaccination within the next ten years.

V.B. Recommendation: *The viability of our nation's adult immunization programs requires evidence of the continued efficacy, safety, clinical effectiveness, cost-benefits and cost-effectiveness of currently available adult vaccines, and research in these areas must be assured adequate support.*

### Findings

Ongoing evaluation of the efficacy, clinical effectiveness, and safety of adult vaccines will be needed if they are to become widely used. Research on the efficacy of current and new vaccines in clinical trials must be complemented by evaluation of their clinical effectiveness in routine use in large populations. Research on the effectiveness of vaccination must emphasize the most important health outcomes that are the goals of vaccination, i.e., the prevention of serious illness and death, not simply infection. Newer methods of research using administrative databases that document health care services for large populations can be especially useful in these studies. These databases can also be used to evaluate the safety of adult vaccines, especially the occurrence of serious adverse events such as Guillain-Barre syndrome following influenza vaccination and chronic arthritis in young women who have received rubella vaccine. Understanding these events requires both epidemiologic and biologic insight into their occurrence and pathogenesis. Finally, the cost-benefits and cost-effectiveness of adult immunization requires much greater attention. For influenza and pneumococcal vaccination, there is already solid evidence that each is highly cost-effective when compared with other interventions used in older adults. Similar studies are needed

for other adult vaccines; for example, the second dose of measles vaccine for certain groups of younger adults, or universal pneumococcal vaccination of all adults if antibiotic resistance to pneumococcal organisms becomes widespread.

### Strategies

- o Continue to evaluate the efficacy and clinical effectiveness of currently available adult vaccines, especially in preventing serious and costly hospitalization and death.
- o Continue to evaluate the safety of adult vaccines, especially their possible association with rare, long-term disabling adverse reactions.
- o Continue to assess the cost-benefits and cost-effectiveness of adult immunization, especially compared with other preventive, screening, and treatment interventions offered to adults.

V.C. Recommendation: *The epidemiology of immunization practices must be better understood if we are to use adult vaccines more effectively and with greater efficiency.*

### Findings

Research on the epidemiology of adult immunization is in most respects an extension of systematic monitoring of the current use of vaccines. However, specific research efforts must be targeted at identifying variations in vaccination practices among health care providers and determining why some providers do so much better than their colleagues. (These differences can be very large; a nine-fold variation in influenza vaccination among British general practitioners has been described recently.) Similarly, investigators must determine whether recommended vaccines are actually being given to those in greatest need. If they are not, new strategies for vaccine delivery must be developed. Vaccine manufacturers must be persuaded that their marketing information, which is epidemiologic in nature, should be used to study important questions related to the epidemiology of adult immunization practice. Such information has already been useful in documenting wide variations in influenza and pneumococcal vaccination in developed countries.

### Strategies

- o Expand research on the epidemiology of adult immunization practices by health care providers, especially geographic variations in vaccine delivery and the characteristics and vaccination behaviors of providers who achieve high rates of vaccine delivery.
- o Expand epidemiologic studies of "missed opportunities" for adult immunization.
- o Study risk factors for vaccine-preventable diseases in relation to vaccination rates in target populations to determine whether adults who are being vaccinated are those at greatest risk of disease.
- o Explore ways of using information on vaccine distribution provided by the manufacturers to provide more detailed understanding of the epidemiology of vaccine delivery.

V.D. Recommendation: *The health benefits of adult immunization with several currently available vaccines will be enhanced by improved vaccines and other diseases will become preventable with new vaccines. Research and development of these vaccines must be assured continued and stable support.*

### Findings

Each year the National Institute of Allergy and Infectious Diseases issues "The Jordan Report" which summarizes progress in the development of new and improved vaccines. The 1993 report documents more than 170 approaches that are being used to develop vaccines against more than 60 target agents of disease. Almost 80 of these approaches have moved beyond the stage of basic research and animal testing and have entered the initial phase of human trials. Approximately 25 new or improved vaccines have entered Phase III testing to establish efficacy and safety. Many of these vaccines will be of potential use in adults, including (1) cold-adapted live-attenuated influenza vaccine; (2) pneumococcal conjugate vaccines; (3) varicella zoster vaccine which should protect against primary varicella virus infection and might prevent reactivation of latent infection as herpes zoster; and (4) several acellular pertussis vaccines which might be used to reduce the reservoir of infection in young adults. Some of these new and improved vaccines will be of importance for both

children and adults worldwide, including those against cholera, malaria, tuberculosis and leprosy. Many of the new approaches to vaccine development involve novel methods of vaccine administration; e.g., newer adjuvants, epitope-based strategies that build on understanding of antigen-recognition sites, particulate antigens delivered as microcapsules, glycoconjugate preparations, immunologic boosting with cytokines and lymphokines, and expanded use of vaccine vectors. Much of the research that is still in its earlier phases is targeted at agents of adult diseases that may one day be preventable; among them, Borrelia burgdoferi (Lyme disease), cytomegaloviruses (of great importance to transplant and HIV-infected patients), enterotoxigenic E. coli (a cause of travelers' diarrhea), and Group B streptococci (for maternal immunization in the third trimester to prevent neonatal sepsis). Research is also directed at broader questions such as the biology of maternal immunization, the immunologic senescence of T helper-1 cells in aging, and the relationships between the genes of the major histocompatibility complex and resistance to infection. The vast array of these investigative efforts involve laboratory and clinical scientists in government, universities, the military, and industry. Collaboration between individuals and institutions is already extensive and is growing, especially with the vaccine manufacturers.

### Strategies

- o Continue federal support for basic and clinical research on new and improved vaccines for adults.
- o Continue federal support for research on new methods for administering vaccines.
- o Continue federal support for studies on the biology and epidemiology of diseases that will become targets for developing, licensing and using new and improved vaccines.
- o Strengthen collaboration between federal agencies and industry regarding research and development of new and improved vaccines.

V.E. Recommendation: Research on all aspects of adult immunization must expand to include other developed and developing countries.

## Findings

The steady increase in the migration of people throughout the world will expand the need for surveillance of vaccine-preventable diseases and for improved vaccines and vaccination programs. For many years the United States has benefitted from information provided by the World Health Organization's Influenza Program. By carefully interpreting antigenic changes in influenza viruses isolated throughout the world, WHO experts have become adept at selecting the virus strains that are most likely to cause epidemic disease. The health benefits the United States has received from this program are almost beyond measure. The eradication of polio in the Western hemisphere is another step along the way toward worldwide eradication of the disease. This, too, has benefitted all Americans.

In spite of these advances, the occurrence of other vaccine-preventable diseases elsewhere in the world will continue to threaten adults in the United States. Measles outbreaks frequently follow importations of disease by young adults who have travelled abroad. The recent emergence of cholera in Peru and its spread to Central America has resulted in its appearance in the southern United States. The transfer of clones of penicillin-resistant Streptococcus pneumoniae from Spain to Iceland raises the possibility that antimicrobial-resistant organisms could become so common in the United States that universal pneumococcal vaccination might be required.

The United States has strong relationships with international and regional health organizations that promote research on childhood vaccines and their delivery in developing countries. Several federal agencies, including the CDC, NIH, FDA, and USAID, work closely with the World Health Organization and the WHO Regional Office for the Americas. Most of these efforts are focused on WHO's Expanded Programme on Immunization (EPI). Officials in the United States also work closely with UNICEF and private organizations such as Rotary International to assist EPI programs. As a result, EPI has recently reported that approximately 80% of children in the developing world who survive the neonatal period now receive all of their basic childhood vaccines.

Several new and improved childhood vaccines will appear in the next few years. It will become increasingly difficult to integrate them into EPI vaccine delivery programs. For this reason, the Children's Vaccine Initiative (CVI) has emerged as the organizing focus to coordinate the transfer of new technologies for vaccine production and vaccine delivery to

developing countries. Under the guidance of its major participating organizations (WHO, USAID, the United Nations Development Program, the World Bank, and the Rockefeller Foundation), the CVI is developing new public-private partnerships to assure the development and transfer of these new technologies.

Many aspects of CVI's program will have implications for the development of new and improved vaccines for adults. In addition, as developing countries achieve high levels of childhood immunization, they will be in a position to consider similar programs for adult immunization. Research will be needed to define the health and economic benefits of adult immunization in developing countries, especially in comparison with other investments in health care technology these countries will inevitably have to consider.

#### Strategies

- o Establish effective collaborative relationships between federal agencies (e.g., CDC, NIH, FDA, USAID) and international organizations (e.g., WHO, UNDP, the World Bank, the Rockefeller Foundation) and regional agencies (PAHO) to promote research on adult vaccines and their use throughout the world.
- o Establish effective liaison with the Children's Vaccine Initiative to ensure that relevant development in childhood vaccines are applied to adult vaccines.
- o Encourage collaborative relationships between nongovernmental and professional organizations in the United States and their international counterparts for research on adult immunization.
- o Develop research programs that explore the potential health benefits and cost-effectiveness of adult ~~immunization for developing and soon-to-be developed~~ countries.

**Table 1.**      **Reported Cases of Vaccine-Preventable Childhood Diseases in the United States.\***

Disease	Maximal No. of Cases (Yr)		1991	% Change
Diphtheria	206,939	(1921)	2	-99.9
Measles	894,134	(1941)	9488	-98.9
Mumps <sup>†</sup>	152,209	(1968)	4031	-97.4
Pertussis	265,269	(1934)	2575	-99.0
Poliomyelitis (paralytic)	21,269	(1952)	0 <sup>‡</sup>	-100.0
Rubella <sup>§</sup>	57,686	(1969)	1372	-97.6
Congenital rubella syndrome	20,000	(1964-1965)	36	-99.8
Tetanus	1,500 <sup>  </sup>	(1923)	49	-96.9

\*Adapted from N Engl J Med 1992; 327:1794-1800.

<sup>†</sup>Mumps first became a reportable disease in 1968.

<sup>‡</sup>Excludes an estimated 5 to 10 cases of vaccine-associated paralysis.

<sup>§</sup>Rubella first became a reportable disease in 1966.

<sup>||</sup>Number of reported deaths.

**Table 2.** Estimated Effect of Full Use of Vaccines Currently Recommended for Adults.\*

Disease	Estimated Annual Deaths (no.)	Estimated Vaccine Efficacy <sup>†</sup> (%)	Current Vaccine Utilization <sup>‡</sup> (%)	Additional Preventable Deaths/Yr <sup>§</sup> (no.)
Influenza	20,000 <sup>¶</sup>	70	41	8,260
Pneumococcal infection	40,000	60	20	19,200
Hepatitis B	5,000	90	10 <sup>¶</sup>	4,050
Tetanus-diphtheria	<25	99	40 <sup>**</sup>	<15
Measles, mumps, and rubella	<30	95	Variable	<30
Travelers' diseases (cholera, typhoid, Japanese encephalitis, yellow fever, poliomyelitis, and rabies)	<10	---	---	<10

\*Adapted from N Engl J Med 1993; 328:1252-8.

<sup>†</sup>Indicates efficacy in immunocompetent adults. Among elderly and immunocompromised patients, estimated efficacy may be lower.

<sup>‡</sup>The percentage of targeted groups who have been immunized according to current recommendations. Rates vary among different targeted groups. Data for influenza and pneumococcal vaccines were obtained from the 1991 National Health Interview Survey and apply to persons  $\geq 65$  years in age.

<sup>§</sup>Calculated as follows: (potential additional vaccine utilization) x (estimated vaccine efficacy) x (estimated annual deaths).

<sup>¶</sup>Variable (range, 0 to 40,000).

<sup>¶</sup>Highly variable (range, 1 percent to 60 percent) among different targeted groups.

<sup>\*\*</sup>This estimate is based on seroprevalence data.

**Table 3.** Target Populations for Childhood and Adult Immunization

	0-4 yrs.	5-19 yrs.	20-64 yrs.	>65 yrs.	>20 yrs.
Total U.S. population (1990 - thousands)	18,757	52,977	145,897	31,079	176,976
Measles	2,814 (15% unvac.) <sup>†</sup>	1,060 (2% unvac.) <sup>‡</sup>	7,295 (5% susc.) <sup>§</sup>	N/A <sup>†</sup>	7,295 (4.1% susc.) <sup>§</sup>
Mumps <sup>†</sup>	2,814 (15% unvac.)	1,060 (2% unvac.)	7,295 (5% susc.)	N/A <sup>†</sup>	7,295 4.1% susc.) <sup>§</sup>
Rubella <sup>††</sup>	2,814 (15% unvac.)	1,060 (2% unvac.)	11,234 (7.7% susc.)	N/A <sup>†</sup>	11,234 (6.3% susc.) <sup>‡‡</sup>
Diphtheria	9,379 (50% unvac.) <sup>†</sup>	2,120 (4% unvac.) <sup>‡</sup>	65,654 (45% susc.) <sup>§§</sup>	15,540 (50% susc.) <sup>§§</sup>	81,194 (45.9% susc.) <sup>§§</sup>
Tetanus	9,379 (50% unvac.) <sup>†</sup>	2,120 (4% unvac.) <sup>‡</sup>	68,572 (47% susc.) <sup>  </sup>	22,688 (73% susc.) <sup>  </sup>	91,260 (52% susc.) <sup>  </sup>
Hepatitis B	Being assessed <sup>¶¶</sup>	-----25,000----- (60% of at-risk pop. susc.) <sup>†††</sup>		N/A <sup>†</sup>	25,000 (60% susc.) <sup>†††</sup>
Influenza <sup>†††</sup>	-----Unknown-----		19,040 (87% of high-risk unvac.)	18,337 (59% unvac.)	37,377 (71% unvac.)
Pneumococcal <sup>§§§</sup>	-----Unknown-----		20,353 (93% of high-risk unvac.)	24,863 (80% unvac.)	45,216 (85% unvac.)

**Table 3. (continued)**

- † CDC, National Health Interview Survey, 1991 (unpublished data).
- \* CDC, school enterer surveys, 1991-92.
- § Summarized from published measles antibody seroprevalence studies among adults.
- ! Not applicable nor calculated given very low disease incidence in this age group.
- ¶ Mumps rates estimated to be the same as for measles.
- †† Rubella rates estimated to be the same as for measles in persons 0-19 yrs.
- ‡ Estimated from CDC seroprevalence study in Hawaii, unpublished data.
- Estimated from diphtheria antitoxin seroprevalence data, National Health and Nutrition Examination Survey I, 1971-75.
- || Estimated from tetanus vaccination coverage within 10 years, National Health Interview Survey, 1991.
- ¶¶ Beginning in 1991, all children in the United States were targeted for hepatitis B vaccination; national coverage levels are being assessed by the National Health Interview Survey in 1993.
- ††† Approximately 41.7 million persons between 5 and 64 years estimated to be at risk for hepatitis B; approximately 25 million (60%) estimated to be susceptible (CDC, unpublished data).
- ‡‡ Only 15% (21,885,000) of persons 20-64 years of age estimated to have high-risk conditions for complications of influenza, and these are the persons recommended to receive the vaccine (CDC, U.S. Immunization Survey, 1985). All persons  $\geq 65$  years of age are recommended to receive the vaccine. Proportion unvaccinated estimated from 1989 and 1991 National Health Interview Surveys.
- §§§ Only 15% (21,885,000) of persons 20-64 years of age estimated to have high-risk conditions for complications of pneumococcal infection, and these are the persons recommended to receive the vaccine (CDC, U.S. Immunization Survey, 1985). All persons  $\geq 65$  years of age are recommended to receive the vaccine. Proportion unvaccinated estimated from 1989 and 1991 National Health Interview Surveys.

**Table 4. Influenza and Pneumococcal Vaccination: Cost-Effectiveness Compared With Other Interventions for Elderly Persons, 1992\***

Intervention		Cost-effectiveness Ratio	QALY or YOLS*
<b>Vaccination</b>	<b>Influenza Pneumococcal</b>	<b>Cost-saving Cost-saving</b>	<b>QALY QALY</b>
Cancer screening	Papanicolaou test, HR, every 3 years	Cost-saving	YOLS
	Mammography	\$ 15,048	YOLS
	Fecal occult blood test, yearly	47,323	YOLS
Heart disease	Beta-blocker after MI	3,495	YOLS
	CABG - left main disease	7,790	QALY
	Lovastatin, HR, known disease	12,500 M <sup>§</sup>	YOLS
	Propranolol - hypertension	15,696	YOLS
	Streptokinase thrombolysis for MI	24,624	YOLS
	Lovastatin, HR, unknown disease	26,250 M	YOLS
	Exercise electrocardiogram	30,750 M	YOLS
Renal disease	Transplantation, living donor	45,877	YOLS
	Hemodialysis	64,762	YOLS

\* Foulds J, Fedson DS. Unpublished observations. HR = high-risk; MI = myocardial infarction; CABG = coronary artery bypass graft surgery.

† The cost-effectiveness ratio usually indicates the additional or marginal costs incurred to achieve a defined outcome with the intervention compared with the costs incurred without the intervention. In the examples cited in the table, influenza and pneumococcal vaccination are cost-saving because the costs of vaccinating all elderly persons are less than the costs of providing medical care to those who develop influenza or pneumococcal disease. In contrast, it costs an additional \$24,624 to add streptokinase thrombolysis to the routine management of elderly patients with acute myocardial infarction. The cost-effectiveness ratios for renal transplantation and hemodialysis are not incremental costs. They are the average costs of achieving an additional year of life.

‡ QALY = quality-adjusted life-year; YOLS = year-of-life saved. A quality-adjusted life-year is a year-of-life saved that takes into account the degree of disability experienced during that year; e.g., a year spent confined to bed is regarded as being of poorer quality than a year of full activity.

§ M = men only. Cost-effectiveness ratios for women are higher.

### Vaccines and toxoids\* recommended for adults, by age groups, United States

Age group (years)	Vaccine/toxoid					Pneumococcal Polysaccharide
	Td <sup>†</sup>	Measles	Mumps	Rubella	Influenza	
18-24	X	X	X	X		
25-64	X	X <sup>‡</sup>	X <sup>‡</sup>	X		
≥65	X				X	X

\*Refer also to sections in text on specific vaccines or toxoids for indications, contraindications, precautions, dosages, side effects, adverse reactions, and special considerations.

<sup>†</sup>Td = Tetanus and diphtheria toxoids, adsorbed (for adult use), which is a combined preparation containing <2 flocculation units of diphtheria toxoid.

<sup>‡</sup>Indicated for persons born after 1956.

### Vaccines and toxoids\* indicated or specifically contraindicated for situations involving special health status, United States

Health situation	Vaccine/toxoid	
	Indicated	Contraindicated
Pregnancy	Tetanus/diphtheria	Live-virus vaccines
Immunocompromised <sup>†</sup>	Influenza Pneumococcal polysaccharide <i>Haemophilus influenzae</i> type b <sup>‡</sup>	Live-virus vaccines Bacille Calmette-Guerin Oral typhoid
Splenic dysfunction or anatomic asplenia	Pneumococcal polysaccharide Influenza Meningococcal polysaccharide <i>Haemophilus influenzae</i> type b <sup>‡</sup>	
Hemodialysis or transplant recipients	Hepatitis B <sup>‡</sup> Influenza Pneumococcal polysaccharide	
Deficiencies of factors VIII or IX	Hepatitis B	
Chronic alcoholism	Pneumococcal polysaccharide	
Diabetes and other high-risk diseases	Influenza Pneumococcal polysaccharide	

\*Refer also to sections in text on specific vaccines or toxoids for details on indications, contraindications, precautions, dosages, side effects and adverse reactions, and special considerations. Unless specifically contraindicated, the vaccines and toxoids recommended for adults are also indicated. See Table 2 for vaccines and toxoids appropriate for most adults, by age.

<sup>†</sup>Recommendations specific to persons infected with human immunodeficiency virus are listed in Table 6.

<sup>‡</sup>May be considered.

\*These patients will need a higher dose or an increased number of doses; see "Hemodialysis and Transplantation" section in text.

**Immunobiologics\* recommended for special occupations, life-styles, environmental circumstances, travel, foreign students, immigrants, and refugees, United States**

Indication	Immunobiologic
Occupation Hospital, laboratory, and other health-care personnel	Hepatitis B Influenza Measles Rubella Mumps Polio
Public-safety personnel	Hepatitis B Influenza
Staff of institutions for the developmentally disabled	Hepatitis B
Veterinarians and animal handlers	Rabies Plague
Selected field workers (those who come into contact with possibly infected animals)	Plague Rabies
Selected occupations (those who work with imported animal hides, furs, wool, animal hair, and bristles)	Anthrax
Life-styles	
Homosexual males	Hepatitis B
Injecting drug users	Hepatitis B
Heterosexual persons with multiple sexual partners or recently acquired sexually transmitted disease	Hepatitis B
Environmental situation	
Inmates of long-term correctional facilities	Hepatitis B
Residents of institutions for the developmentally disabled	Hepatitis B
Household contacts of HBV carriers	Hepatitis B
Homeless persons	Tetanus/diphtheria Measles Mumps Rubella Influenza Pneumococcal polysaccharide
Travel†	Measles Mumps Rubella Polio

**Immunobiologics\* recommended for special occupations, life-styles, environmental circumstances, travel, foreign students, immigrants, and refugees, United States — Continued**

Indication	Immunobiologic
Foreign students, immigrants, and refugees	Influenza
	Hepatitis B
	Rabies
	Meningococcal polysaccharide
	Tetanus/diphtheria <sup>1</sup>
	Yellow fever
	Typhoid
	Cholera
	Plague <sup>1</sup>
	Immune globulin**
	Measles
	Rubella
	Diphtheria
	Tetanus
	Mumps
	Hepatitis B

\*Refer also to sections in text on specific immunobiologics for use by specific risk groups, details on indications, contraindications, precautions, dosages, side effects, and adverse reactions, and special considerations. Unless specifically contraindicated, the vaccines or toxoids recommended for adults are also indicated. Table 2 shows vaccines and toxoids appropriate for most adults by age.

<sup>1</sup>Vaccines needed for travelers will vary depending on individual itineraries; travelers should refer to *Health Information for International Travelers* for more detailed information (see page 11).

<sup>2</sup>If not received within 10 years.

<sup>3</sup>In or during travel to areas with enzootic or epidemic plague in which exposure to rodents cannot be prevented.

\*\*For Hepatitis A prophylaxis.

**Recommendations for routine vaccination of HIV-infected persons\*, United States**

Vaccine/toxoid <sup>†</sup>	HIV infection	
	Known asymptomatic	Symptomatic
DTP/Td	yes	yes
OPV	no	no
eIPV <sup>‡</sup>	yes	yes
MMR	yes	yes <sup>§</sup>
HbCV**	yes	yes
Pneumococcal	yes	yes
Influenza	yes <sup>¶</sup>	yes

\*Appropriate for human immunodeficiency virus (HIV)-infected children and adults.

<sup>†</sup>The vaccine/toxoid abbreviations are defined as follows: DTP = Diphtheria and tetanus toxoids and pertussis vaccine, adsorbed (pediatric); Td = Tetanus and diphtheria toxoids, adsorbed (for adult use); OPV = Oral poliovirus vaccine; eIPV = Enhanced-potency inactivated poliovirus vaccine; MMR = Measles, mumps, and rubella vaccine; HbCV = *Haemophilus influenzae* type b conjugate vaccine; and Pneumococcal = Pneumococcal polysaccharide vaccine.

<sup>‡</sup>For adults ≥18 years of age, use only if indicated. (See text.)

<sup>§</sup>Should be considered.

\*\*May be considered for HIV-infected adults (see "Special Health Status: Conditions that Compromise the Immune System" in text).

# **National Coalition for Adult Immunization (NCAI)\* standards for adult immunization practice, 1990†**

## **The NCAI**

1. Encourages the promotion of appropriate vaccine use through information campaigns for health-care practitioners and trainees, employers, and the public about the benefits of immunizations; and
2. Encourages physicians and other health-care personnel (in practice and in training) to protect themselves and prevent transmission to patients by assuring that they themselves are completely immunized; and
3. Recommends that all health providers routinely determine the immunization status of their adult patients, offer vaccines to those for whom they are indicated, and maintain complete immunization records; and
4. Recommends that all health-care providers identify high-risk patients in need of influenza vaccine and develop a system to recall them for annual immunization each autumn; and
5. Recommends that all health-care providers and institutions identify high-risk adult patients in hospitals and other treatment centers and assure that appropriate vaccination is considered either prior to discharge or as part of discharge planning; and
6. Recommends that all licensing/accrediting agencies support the development by health-care institutions of comprehensive immunization programs for staff, trainees, volunteer workers, inpatients, and outpatients; and
7. Encourages states to establish pre-enrollment immunization requirements for colleges and other institutions of higher education; and
8. Recommends that institutions that train health-care professionals, deliver health-care, or provide laboratory or other medical support services require appropriate immunizations for persons at risk of contracting or transmitting vaccine-preventable illnesses; and
9. Encourages health-care benefit programs, third-party payers, and governmental health-care programs to provide coverage for adult immunization services; and
10. Encourages the adoption of a standard personal and institutional immunization record as a means of verifying the immunization status of patients and staff.

\*Full text of these standards and additional information about the NCAI is available from NCAI, 4733 Bethesda Avenue, Suite 750, Bethesda, MD 20814; telephone (301) 856-0003.

†Member organizations that have endorsed the "Standards" as of September 28, 1990: American Association for World Health; American College Health Association; American College of Physicians; American College of Preventive Medicine; American Indian Health Care Association; American Liver Foundation; American Lung Association; American Medical Association; American Nurses Association; American Podiatric Medical Association; American Public Health Association; American Society for Microbiology; American Society of Hospital Pharmacists; American Society of Internal Medicine; Association for Practitioners in Infection Control; Association of State and Territorial Health Officials; Association of Teachers of Preventive Medicine; Catholic Health Association; CDC; Connaught Laboratories, Inc.; A Pasteur Merieux Company; Harvard Community Health Plan; Health Insurance Association of America; Infectious Diseases Society of America; Lederle-Praxis Biologicals; March of Dimes Birth Defects Foundation; Merck Sharp & Dohme; National Foundation for Infectious Diseases; Pharmaceutical Manufacturers Association; Phi Delta Chi Pharmacy Fraternity; Program for Appropriate Technology in Health (PATH); Service Employees International Union, American Federation of Labor—Congress of Industrial Organizations (AFL-CIO), Central Labor Council; Smith-Kline Beecham Pharmaceuticals; Saint Louis Department of Health and Hospitals; State of Washington Division of Health; U.S. Department of Defense; and Wyeth-Ayerst Laboratories.

## NATIONAL VACCINE ADVISORY COMMITTEE

Report of the Subcommittee on Adult Immunization  
(Dr. Schaffner)

February 1990

The subcommittee formulated its recommendations by addressing a series of barriers to adult immunization.

Recommendations:

1. Financial need should not be a barrier to the immunization of adults.
2. Delivery of immunization services must be adequately reimbursed by Medicaid, Medicare, and private third-party payers.
3. Research should be undertaken into what motivates physicians to offer (and not to offer) vaccines to adults and what motivates persons to accept or decline immunization. The goal is to design effective interventions that will result in behavioral changes leading to increased immunization rates.
4. The public as well as health care professionals should be educated regarding the benefits, risks, and costs of immunizations and the diseases that will be prevented by immunization. There are particular needs to reach certain groups with this information, for example: IV drug users, homosexual men, persons whose residency status is undocumented, older persons, travelers abroad, among others. The educational messages ought to be presented using language and formats that are designed specifically for the group targeted for the educational programs.
5. Standards of care for adult immunization need to be developed by authoritative groups and then promulgated widely.
6. Liability protection should be extended to the use of all vaccines administered to all persons, including adults. Vaccines administered to adults ought to be considered for inclusion in the national vaccine injury compensation system.
7. Research is needed in several areas, among them:
  - o the improvement of existing vaccines, especially influenza vaccine;
  - o the development of rapid and precise diagnostic methods for influenza and pneumococcal disease;
  - o the safety and efficacy of vaccines used in special groups, included but not limited to, pregnant women and persons with AIDS;
  - o the development of new vaccines; and,
  - o persistence of immunity in adults induced by vaccine administered during childhood.
8. An adequate supply of vaccines targeted for use in limited populations must be assured (see Vaccine Supply Subcommittee report).
9. Federal support for adult immunization activities should include reimbursement for clinical services, State immunization grant programs, purchase and distribution of vaccines, evaluation of programs, surveillance of vaccine preventable diseases, surveillance of immunization levels in the general adult population and in special groups, and adverse events monitoring.
10. Support should be provided for the activities of organizations such as (but not limited to) the National Coalition for Adult Immunization, that will coordinate national vaccine policies directed at adults.
11. Legislative and regulatory strategies should be considered to ensure immunization of selected groups of adults.

TERMS OF REFERENCE  
NATIONAL VACCINE ADVISORY COMMITTEE  
SUBCOMMITTEE ON ADULT IMMUNIZATION

1. The membership of the Subcommittee includes National Vaccine Advisory Committee [NVAC] members, the National Vaccine Program [NVP] Office, and NVP agencies. Expert consultation from outside the subcommittee may also be solicited as agreed upon by the Subcommittee Chairman and members.
  2. The Subcommittee will act in an advisory capacity to the NVAC and focus on policy issues related to research and development, safety and efficacy, availability, cost, distribution and use of vaccines for adults in the United States, including special populations at risk. The Subcommittee will examine the means necessary to increase and sustain the use of adult vaccines. The goal is to meet or exceed the targets for vaccine coverage contained in Healthy People 2000.
- Specific issues to be addressed by the Subcommittee will include, but are not limited to:
- a. Identifying impediments to meeting the optimal schedule for recommended vaccines for adults and proposing solutions to overcome them.
  - b. Appropriate roles for the public and private sectors in the delivery of adult vaccines.
  - c. Outreach and promotional activities to improve immunization coverage in adults.
  - d. The adequacy of reimbursement policies for adult vaccinations.
  - e. Legislative options to facilitate adult vaccination.
  - f. Research on vaccine-preventable diseases and diagnosis and on new or improved vaccines for adults.
  - g. Assessment of programs for disease surveillance and vaccine coverage; and assessment of vaccine distribution to ensure adequate availability of adult vaccines.
  - h. The resources available from all sources required to implement the Subcommittee's recommendations.
- The Subcommittee will consider the information and recommendations developed by prior NVAC Subcommittees and other organizations. The goal is to apply aspects of recommendations developed earlier by these groups to improve immunization among adults.

## Appendix V

## Distribution of Vaccines Usually Administered to Adults, United States, 1980-92\*

Year	Tetanus-diphtheria toxoids (Td)	Tetanus toxoid	Influenza vaccine	Pneumococcal vaccine†	Hepatitis B vaccine‡
1980	10,310,850	11,696,607	12,415,890	1,774,000	Not licensed until 1982
1981	10,263,995	9,988,452	19,829,170	2,283,000	
1982	11,309,528	8,530,734	16,959,690	1,153,000	808,000
1983	9,418,149	7,867,613	17,877,970	1,313,000	600,000
1984	11,303,680	8,105,566	19,179,060	1,165,000	705,000
1985	9,519,928	7,318,342	20,700,761	1,276,000	1,080,000
1986	11,390,822	6,165,507	24,226,250§	1,549,059	1,092,000
1987	10,552,940	6,186,045	24,000,811	1,339,663	1,267,392¶
1988	11,500,460	5,791,317	20,243,748	1,407,406	1,738,186
1989	12,716,383	5,549,050	24,410,361	1,175,605	2,012,201¶
1990	11,838,905	3,929,667	25,377,486	1,532,679	3,261,886
1991	12,452,950	4,016,110	30,461,032	2,713,281	3,518,932
1992††	11,562,087	3,042,220	36,848,768	2,555,262	4,901,971††

\* Adapted from CDC Biologics Surveillance System Reports and other references as cited below.

† 1980-85 figures from Fedson DS. Influenza and pneumococcal strategies for physicians. *Chest* 1987;91:436-43.

‡ 1982-86 figures from Merck, Sharp & Dohme (unpublished data).

§ 1986 influenza vaccine figure combines trivalent (18,451,510 doses) and monovalent (5,774,740 doses) vaccine distribution; all other figures are for trivalent vaccine only (no monovalent vaccine distributed).

¶ Only plasma-derived vaccine was distributed from 1982 through 1986. From 1987 through 1990, hepatitis B vaccine distribution included both recombinant and plasma-derived vaccines. Beginning in 1991, only recombinant vaccine has been available in the United States.

¶ In September 1989, Smith-Kline Beecham began distribution of recombinant hepatitis B vaccine, in addition to Merck, Sharp, & Dohme.

†† Estimates based on provisional data as of September 1993.

# Appendix VI

## Vaccine Prices As of August 10, 1993

<u>Vaccine or Product</u>	<u>Packaging</u>	<u>CDC Cost/Dose</u>	<u>Pri. Sector Cost/Dose</u>	<u>Contract End Date</u>	<u>Mfr.</u>
OPV*	50 x 1	\$ 2.1564	\$ 10.427	1/28/94	Led.
E-IPV*	0.5 ml dose x 1	\$ 7.59	\$ 15.74	12/06/93	Conn.
	10 x 1 dose package	\$ 7.59	\$ 14.955	12/06/93	Conn.
DTP*	15 dose vial	\$ 5.89	\$ 10.103	6/17/94	Conn.
DTaP*	15 dose vial	10.01	\$ 16.09	10/25/93	Conn.
DT*	10 dose vial	\$ 0.204	\$ 1.06	6/30/94	Conn.
Td*	10 dose vial	\$ 0.169	\$ 1.06	6/30/94	Conn.
MMR*	1 dose vial x 10	\$ 15.329	\$ 25.29	2/26/94	MSD
Me*	1 dose vial x 10	\$ 9.48	\$ 12.29	2/26/94	MSD
Mu*	1 dose vial x 10	\$ 11.40	\$ 14.70	2/26/94	MSD
Ru*	1 dose vial x 10	\$ 9.16	\$ 13.22	2/26/94	MSD
MR*	1 dose vial x 10	\$ 12.08	\$ 17.64	2/26/94	MSD
	10 dose vial	\$ 6.61	-	2/26/94	MSD
Hib Conjugate	10 dose vial	\$ 5.366	\$ 15.13	3/30/94	Led.
Hib (Booster)	1 dose vial	\$ 4.14	\$ 15.91	3/30/94	Conn.
Hib (Merck)	1 dose vial	\$ 8.25	\$ 14.50	9/13/93	MSD
DTP/HBCV (Tetramune)	1 dose vial x 10		\$ 21.57		Led.
Hepatitis B	0.5 ml vial(1-dose) (pediatric)	\$ 8.20/Dose	\$ 18.00	1/20/94	MSD
	3.0 ml vial(6-dose) (pediatric) (\$ 6.85/Dose)	\$ 41.10/3ml (\$ 6.85/Dose)	\$ 97.00 (\$ 16.17/Dose)	1/20/94	MSD
	1.0 ml vial(1-dose) (adult)	\$ 27.40/ml	\$ 42.83/ml	1/20/94	MSD
	3.0 ml vial(3-dose) (adult) (\$ 27.40/ml)	\$ 82.20/3ml (\$ 27.40/ml)	\$128.50/3ml (\$42.83/ml)	1/20/94	MSD
HBIG	1 ml vial	\$ 34.50/ml	\$ 45.00/ml	4/19/94	NABI
	5 ml vial	\$ 17.20/ml	\$ 30.80/ml	4/19/94	NABI
Pneumococcal Vaccine	5 dose vial	\$ 3.35	\$ 10.028	5/04/94	MSD
Meningococcal (A,C,Y,W135)	1 dose vial	-	\$ 34.75	-	
	10 dose vial	-	\$ 14.60	-	
Yellow Fever	1 dose vial x 5	-	\$ 31.25		

\*Federal Excise Tax included in price as of 8/10/93

Immunobiologics available as of March 1, 1993, by product name and manufacturer, with manufacturers' addresses and telephone numbers.

<u>Immunobiologic</u>	<u>Manufacturer</u>	<u>Product name</u>
Adenovirus vaccine	Wyeth-Ayerst Labs, Inc.	Adenovirus, Live, Oral, Type 4 <sup>*</sup> Adenovirus, Live, Oral, Type 7 <sup>*</sup>
Anthrax vaccine	Michigan Dept. of Public Health	Anthrax Vaccine Adsorbed <sup>**</sup>
BCG vaccine	Organon Teknika Corporation	BCG Vaccine
Cholera vaccine	Wyeth-Ayerst Labs, Inc.	Cholera Vaccine
Cytomegalovirus immune globulin	Massachusetts Public Health Biol Labs	Cytomegalovirus Immune Globulin, Intravenous
Diphtheria and tetanus toxoids adsorbed	Connaught Labs, Inc. A Pasteur-Merieux Company	Diphtheria and Tetanus Toxoids Adsorbed (Pediatric)
	Lederle Laboratories Div. of American Cyanamid Co.	Diphtheria and Tetanus Toxoids Adsorbed (Purogenated for Pediatric Use)
	Massachusetts Public Health Biol Labs	Diphtheria and Tetanus Toxoids Adsorbed (Pediatric)
	Michigan Dept. of Public Health	Diphtheria and Tetanus Toxoids Adsorbed (Pediatric) <sup>**</sup>
	Sciavo SpA <sup>+</sup>	Diphtheria and Tetanus Toxoids Adsorbed, USP (Pediatric)
	Wyeth-Ayerst Labs, Inc.	Diphtheria and Tetanus Toxoids adsorbed (For Pediatric Use)
Diphtheria and tetanus toxoid and acellular pertussis vaccine adsorbed	Connaught Labs, Inc.; A Pasteur-Merieux Company	Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (TRIPEDIA)
	Lederle Laboratories Div. of American Cyanamid Co.	Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (ACEL-IMUNE)
Diphtheria and tetanus toxoids and pertussis vaccine adsorbed	Connaught Labs, Inc. A Pasteur-Merieux Company	Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed
	Lederle Laboratories Div. of American Cyanamid Co.	Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (TRI IMMUNOL)

<u>Immunobiologic</u>	<u>Manufacturer</u>	<u>Product name</u>
	Massachusetts Public Health Biol Labs	Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed
	Michigan Dept. of Public Health	Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed**
<u>Haemophilus influenzae</u> type b vaccine (polysaccharide-conjugate)	Connaught Labs, Inc. A Pasteur-Merieux Company	ProHIBit
	Lederle-Praxis Biologicals	HibTITER
	Merck Sharp & Dohme, Div. of Merck & Co., Inc.	Pedvax-Hib
Hepatitis B Immune globulin	Merck Sharp & Dohme, Div. of Merck & Co., Inc.	Hepatitis B Immune Globulin (Human) (MSD, HEP-B-GAMMAGEE)
	Cutter Biological, Div. of Miles Inc.	Hepatitis B Immune Globulin (HYPER-HEP)
	Abbott Laboratories	Hepatitis B Immune Globulin (Human) (H-BIG)
Hepatitis B vaccine (recombinant)	Merck Sharp & Dohme, Div. of Merck & Co., Inc.	Recombivax HB
	Smith Kline Beecham	Engerix B
Immune globulin	Armour Pharmaceutical Company	Immune Serum Globulin (Human) (GAMMAR; GAMMAR-IV)
	Central Laboratory Blood Transfusion Service, Swiss Red Cross	Immune Globulin Intravenous (SANDOGLOBULIN)
	Cutter Biological, Div. of Miles Inc.	Immune Globulin Intravenous [5% in 10% Maltose (GAMIMUNE)] Immune Globulin (Human), USP (GAMASTAN)
	Hyland Division Baxter Healthcare Corp.	Immune Globulin Intravenous (Human); (GAMMAGARD)
	Massachusetts Public Health Biol Labs	Immune Serum Globulin (Human)
	Michigan Dept of Public Health	Immune Serum Globulin (Human)**
	New York Blood Ctr, Inc.	Immune Serum Globulin (Human)

<u>Immunobiologic</u>	<u>Manufacturer</u>	<u>Product name</u>
Influenza vaccine	Connaught Labs, Inc. A Pasteur-Merieux Company	Influenza Virus Vaccine (Zonal Purified) Whole Virion (FLUZONE)
	Connaught Labs, Inc. A Pasteur-Merieux Company	Influenza Virus Vaccine (Zonal Purified) Split Virion (FLUZONE)
	Lederle Laboratories, Div. of American Cyanamid Co	Influenza Virus Vaccine (Split Virion [FLUIMUNE])
	Parke-Davis, Div. of Warner-Lambert Co.	Influenza Virus Vaccine (Split Virion [FLUOGEN])
	Wyeth-Ayerst Labs, Inc.	Influenza Virus Vaccine, Subvirion Type
Inactivated Japanese encephalitis virus vaccine	Connaught Labs, Inc.; A Pasteur-Merieux Company (U.S. distributor for Biken of Japan)	Inactivated Japanese Enceph- alitis Virus Vaccine (JE-VAX)
Measles, mumps and rubella vaccine	Merck Sharp & Dohme, Div. of Merck & Co., Inc.	Measles, Mumps, and Rubella Virus Vaccine, Live (MSD, MMR II)
Measles and rubella vaccine	Merck Sharp & Dohme, Div. of Merck & Co., Inc.	Measles and Rubella Virus Vaccine, Live (MSD, M-R-VAX II)
Measles vaccine	Merck Sharp & Dohme, Div. of Merck & Co., Inc.	Measles Virus Vaccine, Live (Attenuated [MSD] ATTENUVAX)
Meningococcal polysaccharide vaccine A,C,Y, and W 135	Connaught Labs, Inc. A Pasteur-Merieux Company	Meningococcal Polysaccharide Vaccine (MENOMUNE-A/C/Y/W-135)
Mumps vaccine	Merck Sharp & Dohme, Div. of Merck & Co., Inc.	Mumps Virus Vaccine, Live (MSD, MUMPSVAX)
Pertussis vaccine adsorbed	Michigan Dept. of Public Health	Pertussis Vaccine Adsorbed**
Plague vaccine	Cutter Biological, Div. of Miles Inc.	Plague Vaccine
Pneumococcal polysaccharide vaccine	Lederle Laboratories, Div. of American Cyanamid Co.	Pneumococcal Vaccine, Polyvalent (PNU-IMUNE 23)
	Merck Sharp & Dohme Div. of Merck & Co., Inc.	Pneumococcal Vaccine, Polyvalent (MSD, PNEUMOVAX 23)
Poliovirus vaccine inactivated	Connaught Labs, Inc. A Pasteur-Merieux Company	Poliovax

<u>Immunobiologic</u>	<u>Manufacturer</u>	<u>Product name</u>
Poliovirus vaccine live oral	Lederle Laboratories Div. of American Cyanamid Co.	Poliovirus Vaccine, Live, Oral Trivalent (ORIMUNE)
Rabies immune globulin	Cutter Biological, Div. of Miles Inc.	Rabies Immune Globulin (Human) (HYPERAB)
	Connaught Labs, Inc. A Pasteur-Merieux Company	Rabies Immune Globulin (Human) (IMOGAMRABIES)
Rabies vaccine	Connaught Labs, Inc. A Pasteur-Merieux Company	Rabies Vaccine (Human Diploid Cell [IMOVAX-RABIES], [IMOVAX-RABIES ID])
Rabies vaccine	Michigan Dept. of Public Health	Rabies Vaccine Adsorbed**
Rubella vaccine	Merck Sharp & Dohme, Div. of Merck & Co., Inc.	Rubella Virus Vaccine,, Live (MSD, MERUVAX II)
Rubella and mumps vaccine	Merck Sharp & Dohme, Div. of Merck & Co., Inc.	Rubella and Mumps Virus Vaccine, Live (MSD, BIAVAX II)
Tetanus antitoxin	Sclavp, SpA+	Tetanus Antitoxin Purified, USP
Tetanus immune globulin	Cutter Biological, Div. of Miles Inc.	Tetanus Immune Globulin (Human) (HYPER-TET)
	Massachusetts Public Health Biol Labs	Tetanus Immune Globulin (Human)
Tetanus and diphtheria toxoids adsorbed	Connaught Labs, Inc. A Pasteur-Merieux Company	Tetanus and Diphtheria Toxoids Adsorbed (For Adult Use)
	Lederle Laboratories, Div. of American Cyanamid Co.	Tetanus and Diphtheria Toxoids Adsorbed (For Adult Use) (Purogenated Parenteral)
	Massachusetts Public Health Biol Labs	Tetanus and Diphtheria Toxoids Adsorbed (For Adult Use)
	Sclavo SpA+	Tetanus and Diphtheria Toxoids Adsorbed, USP (Adult)
	Wyeth-Ayerst Labs, Inc.	Tetanus and Diphtheria Toxoids Adsorbed (For Adult Use) [Aluminum Phosphate, Ultrafined]
Tetanus toxoid adsorbed	Connaught Labs, Inc. A Pasteur-Merieux Company	Tetanus Toxoid Adsorbed
	Lederle Laboratories Div. of American Cyanamid Co.	Tetanus Toxoid Adsorbed (Purogenated [Aluminum Phosphate Adsorbed])

<u>Immunobiologic</u>	<u>Manufacturer</u>	<u>Product name</u>
	Massachusetts Public Health Biol Labs	Tetanus Toxoid Adsorbed
	Michigan Dept. of Public Health	Tetanus Toxoid Adsorbed**
	Sclavo SpA+	Tetanus Toxoid Adsorbed, USP
	Wyeth-Ayerst Labs, Inc.	Tetanus Toxoid Adsorbed (Aluminum Phosphate Adsorbed, Ultrafined)
Tetanus Toxoid, fluid	Connaught Labs, Inc. A Pasteur-Merieux Company	Tetanus Toxoid (Fluid)
	Lederle Laboratories Div. of American Cyanamid Co.	Tetanus Toxoid (Purogenated, Tetanus Toxoid Fluid)
	Sclavo SpA+	Tetanus Toxoid (Fluid)
	Wyeth-Ayerst Labs, Inc.	Tetanus Toxoid (Fluid, Purified, Ultrafined)
Typhoid vaccine	Wyeth-Ayerst Labs, Inc.	Typhoid Vaccine, U.S.P.
	Wyeth-Ayerst Labs, Inc.	Typhoid Vaccine* (acetone-killed and dried)
Typhoid vaccine, live oral/Ty21A	Swiss Serum and Vaccine Institute	Vivotif Berna
Vaccinia immune globulin	None (CDC and Dept. of Defense stockpiles only)	Vaccinia Immune Globulin (Human)
Vaccinia vaccine	None (CDC stockpiles only)	Smallpox vaccine
Varicella-zoster immune globulin	Massachusetts Public Health Biol Labs	Varicella-Zoster Immune Globulin (Human) <sup>a</sup>
Yellow fever vaccine	Connaught Labs, Inc. A Pasteur-Merieux Company	Yellow Fever Vaccine (Live, 17D Virus, [YF-VAX])

NOTE: In the preparation of this appendix every effort was made to assure its completeness and accuracy. This appendix was compiled from information obtained from manufacturers, the Division of Product Certification, Food and Drug Administration, and the Physicians Desk Reference, 47th Edition, 1993, and to the best of our knowledge is an accurate and complete listing as of March 1, 1993. However, omissions and errors may have occurred inadvertently. This appendix is intended to be a resource and does not replace the provider's obligation to remain otherwise current on the availability of vaccines, toxoids, and immune globulins.

\*Available only to the U.S. Armed Forces.

\*\*Outside Michigan sold only to providers who will sign a "hold harmless" agreement.

+All Sclavo SpA products' licenses under review by FDA, and may not be available.

<sup>a</sup>Varicella-Zoster immune globulin is available from selected blood banks in various locations in the United States. Consult Update on adult immunization: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1991;40(No.RR-12):89-94.

Immunobiologicals  
Manufacturers/Distributors

<u>Manufacturer/Distributor</u>	<u>Telephone</u>
1. Abbott Laboratories Abbott Park, IL 60064	(708) 937-6100 or (800) 323-9100
2. Armour Pharmaceutical Company Kankakee, IL 60901	(800) 727-6737
3. Connaught Laboratories, Inc. Swiftwater, PA 19370	(717) 839-7189 or (800) 822-2463
4. Cutter Biological Division of Miles Laboratories, Inc. Berkeley, CA 94701	(510) 420-5177 (800) 288-8371
5. Hyland Division Baxter Healthcare Corporation Glendale, CA 91203	(800) 423-2090
6. Lederle Laboratories Division of American Cyanamid Co. Pearl River, NY 10965 Wayne, NJ 07470	(914) 732-5000 (201) 831-2000 (800) 533-3753
7. Lederle-Praxis Biologicals 30 Corporate Woods Suite 300 Rochester, NY 14623	(800) 533-3753 (201) 831-4652
8. Massachusetts Public Health Biologic Laboratories Boston, MA 02130	(617) 522-3700, x276
9. Merck Sharp & Dohme Division Merck & Co., Inc. West Point, PA 19486	(215) 652-5000
10. Michigan Department of Public Health Lansing, MI 48909	(517) 335-8119
11. New York Blood Center Blood Derivatives New York, NY 10021	(212) 570-3000 (800) 487-8751
12. Organon Teknika Corporation 5516 Nicholson Lane Kensington, MD 20895	(800) 323-6442 (800) 842-3220
13. Parke-Davis Division of Warner-Lambert Co. Morris Plains, NJ 07950	(201) 540-2000
14. Sclavo, Inc. Wayne, NJ 07470	(201) 696-8300 or (800) 526-5260
15. Swiss Serum and Vaccine Institute Berna Products Coral Gables, FL 33146	(305) 443-2900 (800) 533-5899
16. Smith Kline Beecham Philadelphia, PA 19101	(215) 751-5231 (800) 366-8900
17. Wyeth-Ayerst Laboratories, Inc. Philadelphia, PA 19101	(800) 321-2304

## Appendix IX-1

### Specific Vaccine-Preventable Diseases of Adults and Adult Vaccines

Vaccine-preventable infections among adults represent a major continuing cause of morbidity and mortality in the United States. The major impact of these infections is in older persons. Effective and safe vaccines against these diseases are available, but they are poorly used. There are several reasons for low vaccination levels among adults. Suboptimal physician and institutional practices have had major influences on vaccine use. Inadequate public awareness of the importance and benefits of vaccination has also been important. Principal causes for the failure to provide vaccines to adults include the failure of health care providers to take advantage of opportunities to immunize adults during office, clinic, and hospital contacts, and the lack of organized programs in medical settings which ensure that adult patients are offered vaccines. Inadequate reimbursement for adult immunization by third-party payers and government agencies, together with the lack of a federal program to support vaccine delivery to adults, have also been major disincentives to adult vaccination. If we are to reach the Public Health Service vaccination goals set for the year 2000, it will be necessary to improve public and provider education and institute major changes in clinical practice and in financial support for adult immunization.

Appendix IX presents a brief synopsis of each of the major vaccine preventable-diseases of adults and their corresponding vaccines. Each synopsis is based on the most recent recommendations of the Advisory Committee on Immunization Practices (ACIP). Information is provided on disease impact, recommendations for vaccine use, and vaccine effectiveness and safety. The appendix includes vaccines that must be considered for all adults and those whose use is limited to special circumstances.

## Appendix IX-2

### Vaccines for All Adults

#### Influenza

Disease Impact. Influenza viruses have continually demonstrated the ability to cause major epidemics of respiratory disease. High attack rates of acute illness and the frequent occurrence of lower respiratory tract complications usually result in dramatic rises in visits to physicians' offices and hospital emergency rooms. Furthermore, influenza frequently affects individuals who, because of their age or underlying health status, are poorly able to cope with the disease and often require medical attention, including hospitalization.

A typical influenza epidemic can cause excess deaths (that is, deaths that would not have occurred in the absence of the epidemic). Increased mortality results not only from influenza and pneumonia, but also from cardiopulmonary and other chronic diseases that can be exacerbated by influenza infection. It is estimated that >10,000 excess deaths occurred during each of seven different U.S. epidemics in the period 1977-1988, and >40,000 excess deaths occurred during each of two of these epidemics. Eighty to ninety percent of these deaths are in persons 65 years of age or older. It has been estimated that well over 200,000 excess hospitalizations occur in each moderate epidemic, at a direct cost of over \$750 million to \$1 billion dollars. The direct and indirect costs of a severe epidemic have been estimated at \$12 billion.

Recommendations for Vaccine Use. Since 1963, annual vaccination against influenza has been recommended for individuals at high risk of lower respiratory tract complications and death following influenza infection (i.e., the elderly and persons with chronic disorders of the cardiovascular, pulmonary, and/or renal systems; metabolic diseases; severe anemia; and/or compromised immune function, including HIV infection). Vaccination is also recommended for persons who may transmit influenza to high-risk persons, including medical personnel, and other persons attending or living with high-risk persons. In addition, influenza vaccine may be offered to persons who provide essential community services, to any adult who wishes to reduce the likelihood of influenza infection, and to the elderly or those with high-risk conditions who travel to areas with active influenza disease.

Vaccine Effectiveness and Safety. The effectiveness of influenza vaccine in preventing or attenuating illness varies, depending primarily on the age and immunocompetence of the vaccine recipient and the degree of similarity between the virus strains included in the vaccine and those that circulate during the influenza season. When there is a good match between vaccine and circulating viruses, influenza vaccine has been shown to prevent illness in approximately 70% of healthy children and younger adults. In these circumstances, studies have also shown that among elderly persons living in the community influenza vaccine can be 30% to 70% effective in preventing hospitalization for pneumonia and influenza due to all causes.

The most frequent side effect of vaccination is soreness at the vaccination site (up to 2 days in fewer than one-third of vaccinees). Fever, malaise, myalgia and other systemic symptoms occur infrequently. Immediate -- presumably allergic -- reactions (such as hives, angioedema, allergic asthma, or anaphylaxis) occur rarely.

## Appendix IX-3

**Pneumococcal**

**Disease Impact.** Pneumococcal disease remains an important cause of morbidity and mortality in the United States. Pneumococcal pneumonia accounts for 10%-25% of all pneumonia cases and an estimated 40,000 deaths annually. Recent studies suggests annual rates of bacteremia of 15-19/100,000 for all persons and 50/100,000 for persons  $\geq 65$  years old. Five percent of patients with pneumonia, 20% of patients with bacteremia, and 30% of patients with pneumococcal meningitis die. For every patient hospitalized with bacteremic pneumococcal pneumonia there are five to ten times as many patients hospitalized with nonbacteremic disease. The risks for complications, hospitalization and death are highest among patients with underlying medical conditions and older persons.

**Recommendations for Vaccine Use.** Vaccination for pneumococcal disease is recommended for persons  $\geq 65$  years old, those with chronic illnesses (such as cardiovascular and pulmonary disease, diabetes mellitus, cirrhosis, cerebrospinal fluid leaks, or alcoholism), and immunocompromised adults (such as persons with splenic dysfunction or anatomic asplenia, hematologic malignancies, chronic renal failure, nephrotic syndrome, or conditions associated with immunosuppression). Revaccination should be strongly considered  $\geq 6$  years after the first dose for those at highest risk for fatal pneumococcal infection (e.g., asplenic patients) and for those at risk of rapid decline in antibody levels (e.g., persons with chronic renal failure, nephrotic syndrome, or transplanted organs). Most patients who receive pneumococcal vaccine should also be vaccinated with influenza vaccine, which can be given simultaneously at a different site.

**Vaccine Effectiveness and Safety.** The duration of vaccine-induced immunity is unknown. Studies of persistence of vaccine-induced antibody show elevated titers 5 years after vaccination among healthy adults. Estimates of pneumococcal vaccine efficacy have varied widely in several studies. Studies based on CDC's pneumococcal surveillance system suggest an efficacy of 60%-64% for vaccine-type strains in patients with bacteremic disease. For all persons  $\geq 65$  years of age, vaccine efficacy was 44%-61%. Case-control studies that have emphasized complete ascertainment of vaccination status suggest a range of efficacy against pneumococcal bacteremia from 61% to 81%.

About half of the persons given pneumococcal vaccine experience mild side effects such as erythema and pain at the site of injection. Fever, myalgias, and severe local reactions have been reported by fewer than 1% of those given vaccine. Severe systemic reactions, such as anaphylaxis, have rarely been reported. A similar incidence of adverse events after primary vaccination and revaccination has been noted among adults when revaccination occurs  $>4$  years after primary vaccination.

## Appendix IX-4

**Hepatitis B**

**Disease Impact.** The estimated lifetime risk of acquiring hepatitis B virus (HBV) infection in the United States is approximately 5% for the population as a whole but may approach 100% for persons at highest risk. An estimated 200,000-300,000 HBV infections occur in the United States each year, leading to approximately 10,000 hospitalizations and 250 deaths due to fulminant hepatitis B. Between 6% and 10% of adults with HBV infection become carriers. The estimated 1 million-1.25 million persons with chronic HBV infection United States are potentially infectious to others, and many are at risk for long-term sequelae such as chronic liver disease and primary hepatocellular carcinoma. Each year approximately 4,000-5,000 persons die from HBV-related chronic liver disease.

**Recommendations for Vaccine Use.** Immunization is recommended for adults at increased risk of occupational, social, family, environmental, or illness-related exposure to HBV. These include homosexual males, users of illicit injectable drugs, heterosexual persons with multiple partners or other sexually transmitted diseases, household and sexual contacts of HBV carriers, workers in health-related and public-safety occupations requiring frequent exposure to blood, residents and staff of institutions for the developmentally disabled, hemodialysis patients, recipients of factor VIII or IX concentrates, and morticians and their assistants. Inmates in some long-term correctional facilities may also be candidates for vaccination. Vaccination should also be considered for persons who plan to reside for more than 6 months in areas with high levels of endemic HBV and who will have close contact with the local population and for travelers intending a short stay who are likely to have contact with blood from or sexual contact with residents of areas with high levels of endemic disease.

**Vaccine Effectiveness and Safety.** Clinical trials of the hepatitis B vaccines licensed in the United States have shown that they are 80%-95% effective in preventing HBV infection and clinical hepatitis among susceptible adults. If a protective antibody response develops after vaccination, vaccine recipients are virtually 100% protected against clinical illness. Long-term studies of healthy adults indicate that immunologic memory remains intact for at least 10 years and confers protection against chronic HBV infection, even though anti-HBs levels may become low or decline below detectable levels.

The most common side effect observed following vaccination with each of the available vaccines has been soreness at the injection site. Postvaccination surveillance for three years after licensure of the plasma-derived vaccine showed an association of borderline significance between Guillain-Barre syndrome (GBS) and receipt of the first vaccine dose. The rate of this occurrence was very low (0.5 per 100,000 vaccinees). Such postvaccination surveillance information is not available for the recombinant HB vaccines.

## Appendix IX-5

**Diphtheria and Tetanus**

**Disease Impact.** Vaccination of children against diphtheria and tetanus and careful wound management has reduced the occurrence of these diseases by 90% or more. The remaining problem involves unimmunized and inadequately immunized adults. Nearly all of the one to five cases of diphtheria reported each year in the United States occur in unimmunized adults. More than 70% of the 50 to 60 cases of tetanus reported annually occur in persons 50 years of age and older; over 90% have never received a primary series of tetanus toxoid or have unknown vaccination status. Age-specific incidence rates of tetanus increase progressively by age and are eight-fold or more higher among persons 60 and older compared to 20 to 29 year olds. Case-fatality rates may exceed 40% in older age groups, despite medical care.

**Recommendations for Toxoid Use.** All adults lacking a completed primary series of tetanus and diphtheria toxoids should complete the series with Td. A primary series for adults is three doses of preparations containing tetanus and diphtheria toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second. All adults for whom 10 years or more have elapsed since completion of their primary series or since their last booster dose should receive a dose of Td. Thereafter, a booster dose of Td should be administered every 10 years. There is no need to repeat doses if the schedule for the primary series or booster doses is delayed.

**Toxoid Effectiveness and Safety.** Complete and appropriately timed vaccination is at least 85% effective in preventing diphtheria and nearly 100% effective in preventing tetanus. Td is the preferred preparation for active diphtheria and tetanus immunization of adults because a large proportion also lack protective levels of circulating antitoxin against both diphtheria and tetanus. Evidence indicates that complete primary vaccination with tetanus and diphtheria toxoids provides long-lasting protection--10 years or more in most recipients. For wound management the need for active immunization, with or without passive immunization with tetanus immune globulin, depends on the condition of the wound and the patient's vaccination history. Only rarely have cases of tetanus occurred in persons with a documented primary series of toxoid injections. For clean and minor wounds occurring during the 10-year interval no additional booster is recommended. For other wounds, a booster is appropriate if the patient has not received tetanus toxoid within the preceding 5 years. Persons who have not completed a full primary series or whose vaccination status is unknown or uncertain may require tetanus toxoid and passive immunization at the time of wound cleaning and debridement.

Local reactions, generally erythema, and induration, with or without tenderness, can occur after Td is administered. Fever and other systemic symptoms are less common. Arthus-type hypersensitivity reactions, characterized by severe local reactions generally starting 2-8 hours after an injection and often associated with fever and malaise may occur, particularly in persons who have received multiple boosters of T toxoid. Rarely, severe systemic reactions such as generalized urticaria, anaphylaxis, or neurologic complications have been reported.

## Measles

**Disease Impact.** Measles is often a severe disease, complicated by middle ear infection or bronchopneumonia. Encephalitis occurs approximately one of every 1,000 reported cases; survivors of this complication often have permanent brain damage and mental retardation. Death, usually from respiratory and neurologic causes, occurs in one of every 1,000 reported measles cases. The risk for encephalitis is greater in adults than in other age groups and, aside from infants, the highest case-fatality rate occurs in adults. Measles during pregnancy leads to increased rates of premature labor, spontaneous abortion, and low-birth-weight infants.

Since vaccine licensure in 1963, the collaborative efforts of public and private health care providers have resulted in a 99% reduction in the reported incidence of measles. Importations still occur, however, and there is continuing risk for exposure, particularly for health care workers and young adults attending college or traveling abroad. Outbreaks continue to be reported from places where young adults congregate, such as colleges and universities.

**Recommendations for Vaccine Use.** Measles vaccine is indicated for all adults born in or after 1957 who lack documentation of physician-diagnosed measles, laboratory evidence of measles immunity, or documentation of adequate vaccination. Persons vaccinated with live measles vaccine before their first birthday, those who received measles vaccine of unknown type between 1963 and 1967 or further attenuated measles vaccine accompanied by immune globulin or measles immune globulin, and those vaccinated with inactivated vaccine followed within 3 months by live vaccine, should be considered unvaccinated. Special efforts should be made to ensure immunity of persons entering college, beginning employment in medical facilities, or planning international travel. Two doses of measles vaccine are recommended for these groups.

**Vaccine Effectiveness and Safety.** Measles vaccine produces a mild or inapparent noncommunicable infection. A single subcutaneously administered dose of live measles vaccine provides durable protection against measles in 95% or more of recipients vaccinated at 15 months or older, extending probably for their lifetime. MMR is the vaccine of choice.

A temperature of 103 F (39.4 C) or higher may develop in about 5%-15% of vaccinees, generally beginning between days 5 and 12 after vaccination; fever usually lasts 1-2 days and, rarely, up to 5 days. Rashes have been reported in approximately 5% of vaccinees. Encephalitis following measles vaccination is extremely rare. Its incidence can not be discerned from the background incidence rate of encephalitis of unknown etiology and is much lower than that following natural measles.

Reactions after live measles vaccination occur in 4%-55% of prior recipients of killed measles vaccine. The reactions are generally mild, consisting of a local reaction with or without a low-grade fever of 1-2 days' duration. Such reactions can be fairly severe, but are milder than atypical measles syndrome, an illness that may affect prior recipients of killed measles vaccine who are exposed to natural measles.

## Appendix IX-7

**Mumps**

Disease Impact. Although mumps is generally self-limited, meningeal signs may appear in up to 15% of cases, and orchitis in 20%-30% of clinical cases among postpubertal males. Although some testicular atrophy occurs in about 35% of cases of mumps orchitis, sterility is a rare sequela. Reported rates of mumps encephalitis range as high as five cases per 1000 reported mumps cases. Permanent sequelae are rare, but the reported encephalitis case-fatality rate has averaged 1.4%. Unilateral sensorineural deafness occurs at a rate of one case per 20,000 cases of mumps. Mumps infection during the first trimester of pregnancy may increase the rate of spontaneous abortion (reported to be as high as 27%). Although overall mortality is low, death due to mumps infection is much more likely to occur in adults; about half of mumps associated deaths have been in persons  $\geq 20$  years old.

The reported occurrence of mumps cases in the United States has decreased steadily since the introduction of live mumps-virus vaccine. In 1985, a record low of 2,982 cases was reported; this number represented a 98% decline from the 185,691 cases reported in 1967, the year live mumps vaccine was licensed. However, between 1985 and 1987, a relative resurgence of mumps occurred, with 7,790 cases reported in 1986 and 12,848 cases in 1987. Mumps incidence increased in all age groups during this period, but the most dramatic increases were among 10-14-year-olds (a seven-fold increase) and 15-19-year olds (a more than eight-fold increase). Reported mumps has generally continued to decline since 1987, but has fluctuated from a high in 1989 of 5,712 cases to a low of 2,572 in 1992. During this period, age-specific incidence continued to be highest among those 10-19 years of age.

Recommendations for Use. Mumps vaccine is indicated for all adults believed to be susceptible. Persons should be considered susceptible to mumps unless they have documentation of physician-diagnosed mumps, adequate immunization with live mumps-virus vaccine on or after their first birthday, or laboratory evidence of immunity. Most adults born before 1957 are likely to have been infected naturally and generally can be considered immune, even if they did not have clinically recognizable mumps disease. Persons who are unsure of their history of mumps disease and/or mumps vaccination should be vaccinated.

Vaccine Effectiveness and Safety. Live mumps vaccine is approximately 95% efficacious in preventing mumps; >97% of susceptible persons develop measurable antibody following vaccination. Vaccine-induced antibody is protective and long-lasting, although of considerably lower titer than antibody resulting from natural infection. Reported clinical vaccine efficacy ranges between 75% and 95%. MMR is the vaccine of choice if recipients are likely to be susceptible to measles and/or rubella as well as to mumps.

Parotitis and fever after vaccination have been reported rarely. Allergic reactions including rash, pruritus, and purpura have been associated temporally with mumps vaccination, but are uncommon, usually mild, and of brief duration. The frequency of reported central nervous system (CNS) dysfunction following mumps vaccination is not greater than the observed background incidence rate in the general population.

## Appendix IX-8

**Rubella**

**Disease Impact.** The number of reported rubella cases has decreased steadily from over 56,000 cases in 1969, the year rubella vaccine was licensed, to 160 cases in 1992, an all-time low. Until the mid-1970s, the strategy was to vaccinate all children; this approach dramatically reduced the incidence of rubella, but had less impact on older age groups, resulting in an increased proportion of cases in adolescents and adults. From 1988 to 1990, the incidence of rubella increased most for persons aged 15 to 29 years and for those over 30. Cases reported in 1991 were primarily persons <30 years of age, reflecting outbreaks which occurred in religious communities who refused vaccination and had low vaccination levels among children and young adults. A cluster of at least 11 were born in 1990, representing the outcome of many outbreaks that occurred in settings in which adolescents and adults congregate. The majority of the 47 cases of CRS reported in 1991 followed the outbreaks in religious communities. Efforts to increase delivery of vaccine to college-age and older persons have led to the current decline in the incidence rates for these age groups. However, an estimated 6%-11% of young adults remain susceptible to rubella, and limited outbreaks continue to be reported in universities, colleges, and places of employment--notably hospitals.

**Recommendations for Vaccine Use.** Preventing fetal infection and consequent CRS are the objectives of rubella immunization. Rubella vaccine is recommended for adults, particularly females, unless proof of immunity is available (i.e., documented rubella vaccination on or after the first birthday or positive results from a serologic test) or unless the vaccine is specifically contraindicated. In particular, nonpregnant susceptible women of childbearing age should be provided rubella vaccination a) during routine internal medicine and gynecologic outpatient care, b) during routine care in a family planning clinic, c) following premarital screening, d) before discharge from a hospital for any reason, and e) after childbirth or termination of pregnancy. In addition, evidence of rubella immunity should be required for all individuals in colleges and universities and all hospital personnel (male and female) who might be at risk of exposure to patients infected with rubella or who might have contact with pregnant patients or personnel. All women travelers, particularly those of childbearing age, should also be immune before leaving the United States.

**Vaccine Effectiveness and Safety.** A single dose of live attenuated rubella vaccine provides long-term, probably lifetime, immunity in approximately 95% of vaccinees. Moreover, there has been no identified transmission of vaccine virus in studies of >1200 susceptible household contacts of vaccinees and in over 20 years of experience with live rubella vaccine.

Vaccinees can develop low-grade fever, rash, and lymphadenopathy after vaccination. Up to 25% of susceptible postpubertal female vaccinees have had arthralgia after vaccination, and signs and symptoms of arthritis occur transiently in 10% of recipients. Arthralgia and transient arthritis occur more frequently and tend to be more severe in susceptible women than in seropositive women and children. When joint symptoms or other types of pain and paresthesias do occur, they generally begin 1-3 weeks after vaccination, persist for 1 day to 3 weeks, and rarely recur. Adults with joint

## Appendix IX-9

problems usually have not had to interrupt work activities. There have been sporadic case reports of persistent joint symptoms among susceptible vaccinees, primarily adult women. Although one group of investigators has reported the frequency of chronic joint symptoms and signs in adult women to be as high as 5%-11%, other data from the United States and experience from other countries that use the RA 27/3 vaccine virus strain suggest that such phenomena are rare. In comparative studies, the frequency of chronic joint complaints is substantially higher following natural infection than following vaccination. Complaints of transient peripheral neuritis such as paresthesias and pain in the arms and legs have occurred very rarely and only in susceptible vaccinees; these symptoms rarely persist.

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## Appendix IX-10

## Vaccines for Use in Special Circumstances

**Poliomyelitis**

Disease Impact. The risk of poliomyelitis is very small in the United States; however, epidemics could occur if the high immunity level of the general population is not maintained by vaccinating children routinely or if wild poliovirus is introduced into susceptible populations in communities with low immunization levels. There have been no indigenous cases of wild-type polio in the United States since 1979. In the United States inapparent infection with wild poliovirus strains no longer contributes significantly to establishing or maintaining immunity. Most adults are already immune.

Recommendations for Vaccine Use. Two types of poliovirus vaccines are currently licensed in the United States: live-attenuated oral polio vaccine (OPV) and enhanced-potency inactivated polio vaccine (eIPV). In general, it is not necessary to vaccinate adults living in the United States who have not had a primary series as children. However, adults who have not had a primary series and who are at greater risk than the general population of exposure to wild polioviruses because of foreign travel or health occupation should be vaccinated. Vaccination with eIPV is preferred since the risk of OPV-associated paralysis is slightly higher in adults than in children.

For previously unvaccinated adult travelers, if less than 4 weeks is available before protection is needed, a single dose of OPV or eIPV is recommended. Travelers who have previously received less than a full primary course of OPV or IPV should be given the remaining required doses of either vaccine, regardless of the interval since the last dose and the type of vaccine previously received. Travelers to developing countries who have previously completed a primary series of OPV should receive a single dose of OPV. Additional booster doses of OPV are probably not necessary. Those who have previously received a primary series of IPV should receive a dose of either OPV or eIPV. Health-care personnel in close contact with patients who may be excreting wild polioviruses, and laboratory personnel handling specimens that may contain wild polioviruses should have completed a primary series of poliovirus vaccine. eIPV is indicated because of the slightly increased risk to adults of vaccine-associated paralysis after OPV administration, and since virus may be shed after receipt of OPV and inadvertently expose susceptible immunocompromised contacts to vaccine virus.

Vaccine Effectiveness and Safety. A primary vaccination series with either OPV or eIPV produces immunity to all three types of poliovirus in more than 95% of recipients. No serious side effects of currently available eIPV have been documented. Since eIPV contains trace amounts of streptomycin and neomycin, persons with signs and symptoms of an anaphylactic reaction (e.g., hives, swelling of mouth and throat, difficulty in breathing, hypotension, or shock) following receipt of streptomycin or neomycin should not receive eIPV. In rare instances, administration of OPV has been associated with paralysis in healthy recipients and their contacts. The risk of vaccine-associated paralytic poliomyelitis is extremely small for immunologically normal vaccinees (approximately one case per 1.2 million first doses distributed, and one case per 116.5 million subsequent doses) and for their susceptible, immunologically normal household contacts (approximately one case per 1.0 million first doses distributed, and one case per 25.9 million subsequent doses). However, all vaccinees should be informed of this risk.

## Appendix IX-11

**Rabies**

Disease Impact. Although rabies rarely affects humans in the United States, approximately 10,000 persons receive rabies vaccine every year for postexposure prophylaxis, and an additional 18,000 persons receive preexposure prophylaxis. The likelihood of human exposure to rabies from domestic animals has decreased greatly in recent years. In every year since 1976, more than 85% of all reported cases of animal rabies have been among wild animals, the most important source of possible infection for humans in the United States. For persons traveling overseas to developing countries with endemic rabies, however, the dog remains the animal most likely to transmit rabies.

Recommendations for Vaccine Use. Two inactivated rabies vaccines are currently licensed for preexposure and postexposure prophylaxis in the United States: Rabies vaccine, Human Diploid Cell (HDCV); and Rabies Vaccine, Adsorbed (RVA). Preexposure immunization should be considered for high-risk groups: animal handlers, certain laboratory workers and field personnel, and persons planning to spend more than 1 month in areas of countries where rabies is a constant threat. Persons whose vocations or avocations bring them into contact with potentially rabid animals, including skunks, raccoons and bats, should also be considered for preexposure vaccination. Persons with continuing risk of exposure should receive a booster dose every 2 years; or they should have their serum tested for rabies antibody every 2 years and, if the titer is inadequate, receive a booster dose. The decision to provide postexposure antirabies treatment should include consideration of (1) type of exposure, (2) species of biting animal, and circumstances of the biting incident.

Vaccine Effectiveness and Safety. Evidence from laboratory and field experience in many areas of the world indicates that postexposure prophylaxis combining local wound treatment, passive immunization, and vaccination is effective when appropriately applied. Preexposure vaccination does not eliminate the need for additional therapy after a rabies exposure, but does simplify therapy by eliminating the need for rabies immune globulin and decreasing the number of vaccine doses needed. Local reactions, such as pain, erythema, and swelling or itching at the injection site are reported by up to 74% of recipients. Mild systemic reactions such as headache, nausea, abdominal pain, muscle aches, and dizziness are reported by between 5% and 40% of recipients. After primary vaccination, systemic allergic reactions ranging from hives to anaphylaxis occur in an estimated 11 of 10,000 vaccinees. Following booster doses, mild immune-complex-like hypersensitivity reactions consisting of hives, itching, and angioedema occur 2-21 days later in about 6% of recipients and are the most frequently reported allergic reactions. Fewer than 1% of persons develop such reactions following primary administration of HDCV. Two cases of neurologic illness resembling GBS that resolved without sequelae in 12 weeks have been reported as well as a number of different subacute central and peripheral nervous system disorders temporally associated with HDCV vaccine, but a causal relationship has not been established.

## Appendix IX-12

## Typhoid

**Disease Impact.** The incidence of typhoid fever declined steadily in the United States from 1900 to 1960 and has since remained at a low level. From 1975 through 1989, the average number of cases reported annually was 447. During the years 1975-1989, 59% of cases for which the patient's age was known occurred in patients 20 years of age or older. The majority of typhoid cases reported in the United States are acquired by travelers to other countries.

**Recommendations for Vaccine Use.** Vaccination is indicated for travelers to areas where a recognized risk of exposure to typhoid exists, although no country requires typhoid immunization for entry. Vaccination is particularly recommended for travelers who will have prolonged exposure to potentially contaminated food and water in smaller villages or rural areas off the usual tourist routes. Two other groups for whom selective vaccination is indicated are persons with intimate exposure (i.e., continued household contact) to a documented typhoid carrier, and workers in microbiology laboratories who frequently work with *Salmonella typhi*. Typhoid vaccination is not recommended in the United States for use in areas of natural disaster.

**Vaccine Effectiveness and Safety.** Two typhoid vaccines are available for civilian use in the United States: (1) an oral live-attenuated vaccine (Ty21a strain of *Salmonella typhi*); and, (2) a parenteral heat-phenol-inactivated vaccine that has been widely used for many years. A third capsular polysaccharide vaccine (ViCPS) may be licensed soon for parenteral use. In controlled field trials conducted among Chilean schoolchildren, three doses of the Ty21a vaccine were shown to reduce laboratory-confirmed infection by 67% for at least 4 years. In a subsequent trial, 3 doses provided 33% protection overall; when stratified by age, persons  $\geq 10$  years old had 53% protection. Efficacy of vaccination with Ty21a vaccine has not been demonstrated for persons from areas without endemic disease who travel to endemic-disease regions. In two field trials involving a primary series of two doses of heat-phenol-inactivated vaccine, vaccine efficacy ranged from 51%-76%. A single injection of the new capsular polysaccharide (ViCPS) vaccine produced seroconversion ( $\geq 4$ -fold rise in titers) in 83%-98% of healthy United States adult volunteers. Two field trials in endemic areas have demonstrated efficacy in preventing typhoid fever; one dose provided 74% protection for 20 months in persons aged 5-44 years in one study, and 55% protection in 5-15 year olds for three years in the other study. Efficacy of vaccination with ViCPS has not been demonstrated for persons from areas without endemic disease who travel to endemic-disease regions.

Inactivated typhoid vaccine often results in 1-2 days of discomfort at the site of injection. The local reaction may be accompanied by fever (14%-29% of vaccinees) and headache (9%-30%). More severe reactions have been sporadically reported, including hypotension, chest pain, and shock. Adverse reactions from the oral typhoid vaccine reported to the manufacturer occurred at a rate of  $< 1/100,000$  doses administered. Reactions reported consisted of nausea, abdominal cramps, vomiting, and skin rash or urticaria. In a direct comparison, ViCPS produced reactions less than half as frequently as parenteral inactivated vaccine.

## Appendix IX-13

**Yellow Fever**

**Disease Impact.** Cases of yellow fever are reported only from Africa and South America. Two forms of yellow fever--urban and jungle--are distinguishable epidemiologically. Clinically and etiologically they are identical. Urban yellow fever is an epidemic viral disease transmitted from infected to susceptible persons by the Aedes aegypti mosquito. Ae. aegypti breed in domestic and nearby containers (e.g., water jars, barrels, drums, tires, tin cans) and thus in close association with humans. In areas where the Ae. aegypti mosquito has been eliminated or suppressed, urban yellow fever has disappeared. Jungle yellow fever is an enzootic viral disease transmitted among nonhuman hosts by a variety of mosquito vectors. It is currently observed only in forested areas of South America and forest-savannah zones of tropical Africa, but occasionally extends into Central America and the island of Trinidad and may far exceed the zones officially reported to be infected. In South America 100-300 cases are recognized annually, mainly among persons with occupational exposure in forested areas. In Africa, sporadic endemic cases and epidemics that affect thousands of persons are spread by forest mosquito vectors.

**Recommendations for Vaccine Use.** Vaccination is recommended for persons traveling or living in areas where yellow fever infection occurs--currently parts of Africa and Central and South America. Information on known or probably infected areas is published annually in CDC's Health Information for International Travel. Countries currently reporting yellow fever are noted biweekly in CDC's Summary of Health Information for International Travel. All state health departments and many county and city health departments receive these publications. Some countries, especially in Africa, require evidence of vaccination from all entering travelers. Other countries may waive the requirements for travelers coming from noninfected areas and staying less than 2 weeks. Some countries require a traveler, even if only in transit, to have a valid certificate if the traveler has visited any country thought to harbor yellow fever virus. Vaccination is also recommended for laboratory personnel who might be exposed to virulent yellow fever virus. Booster doses are needed at 10-year intervals.

**Vaccine Effectiveness and Safety.** The yellow fever vaccine available in the United States is an attenuated, live-virus vaccine prepared from the 17D strain of virus grown in chick embryos. The vaccine is highly effective against both the urban and jungle forms of the disease. Immunity is induced by a single injection of reconstituted vaccine and persists for more than 10 years. For international travel, yellow fever vaccine produced by different manufacturers worldwide must be approved by WHO and administered and certified at an approved Yellow Fever Vaccination Center.

Reactions to 17D yellow fever vaccine are generally mild. From 2% to 5% of vaccinees have mild headache, myalgia, low-grade fever, or other minor symptoms 5-10 days after vaccination. Fewer than 0.2% curtail regular activities. Immediate hypersensitivity reactions, characterized by rash, urticaria, and/or asthma, are extremely uncommon and occur principally in persons with a history of egg allergy. Although more than 34 million doses of vaccine have been distributed, only two cases of encephalitis temporally associated with vaccinations have been reported in the United States; in one fatal case, 17D virus was isolated from the brain.

## Appendix IX-14

**Meningococcal**

**Disease Impact.** Meningococcal disease is endemic throughout the world but may also occur in epidemics. Among U.S. civilians, meningococcal disease occurs primarily as single, isolated cases or, infrequently, in small, localized clusters. One third of all cases of meningococcal disease occur in patients 20 years old or older. Serogroup B and C strains cause the majority of U.S. cases, with serogroups Y and W135 accounting for most of the remainder.

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**Recommendations for Vaccine Use.** Vaccine may be of benefit for travelers to areas with epidemic meningococcal disease. Vaccine may also be used in aborting and controlling outbreaks caused by serogroups represented in the vaccine. In addition, it is recommended for individuals with terminal complement component deficiencies and those with anatomic or functional asplenia. The need for booster doses has not been established.

In the United States routine vaccination of civilians with meningococcal polysaccharide vaccine is not recommended because of the lack of availability of a group B vaccine and the low overall risk of infection.

**Vaccine Effectiveness and Safety.** One meningococcal polysaccharide vaccine, a quadrivalent A, C, Y, and W135 vaccine, is available for use in the United States. It is given as a single dose, and induces serogroup specific immunity. The duration of immunity conferred by the vaccine is not known. The serogroup A vaccine has been shown to have a clinical efficacy of 85%-95% and to be of use in controlling epidemics. A similar level of clinical efficacy has been demonstrated for the serogroup C vaccine. The group Y and W-135 polysaccharides have been shown to be safe and immunogenic in adults; clinical protection has not been demonstrated directly, but vaccination induces bactericidal antibody.

Adverse reactions to meningococcal polysaccharide vaccine are infrequent and mild, consisting principally of localized erythema lasting 1-2 days.

## Appendix IX-15

**Cholera**

**Disease Impact.** Cholera continues to be a health risk in Africa, Asia, and South America. Persons who follow the usual tourist itinerary and who use tourist accommodations in countries affected by cholera are at virtually no risk of infection. Infection is acquired primarily by consuming contaminated water or food; person-to-person transmission is rare. The traveler's best protection against cholera is avoiding food and water that might be contaminated.

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**Recommendations for Vaccine Use.** Cholera vaccine is indicated for travelers to countries requiring evidence of cholera vaccination for entry. In addition, the complete primary series is suggested only for special high-risk groups that live under less than sanitary conditions in areas in which cholera is highly endemic. Boosters may be given every 6 months if required by a country.

The risk of cholera to most U.S. travelers is so low that it is doubtful that vaccination is of benefit. WHO no longer recommends cholera vaccination for travel to or from cholera-infected areas. However, some countries affected or threatened by cholera may require evidence of cholera vaccination as a condition of entry. Current information on cholera-vaccination requirements of individual countries is published annually in CDC's Health Information for International Travel. All state health departments and many county and city health departments receive this publication. Travelers to countries with cholera-vaccination requirements should have an International Certificate of Vaccination filled in, dated, signed, and validated, showing receipt of the vaccine 6 days to 6 months before entry into the country. Most city, county, and state health departments can validate certificates. Failure to secure validation may cause travelers to be revaccinated or quarantined upon entry to a country requiring vaccination.

**Vaccine Effectiveness and Safety.** The currently available cholera vaccine has been shown in field trials to be only about 50% effective in preventing clinical illness for a period of 3-6 months. The vaccine does not prevent transmission of infection.

Vaccination often results in 1-2 days of pain, erythema, and induration at the site of injection. The local reaction may be accompanied by fever, malaise, and headache. Serious reactions, including neurologic reactions, following cholera vaccination are extremely rare.

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